



Distinguishing Emotional Dysregulation from Mania

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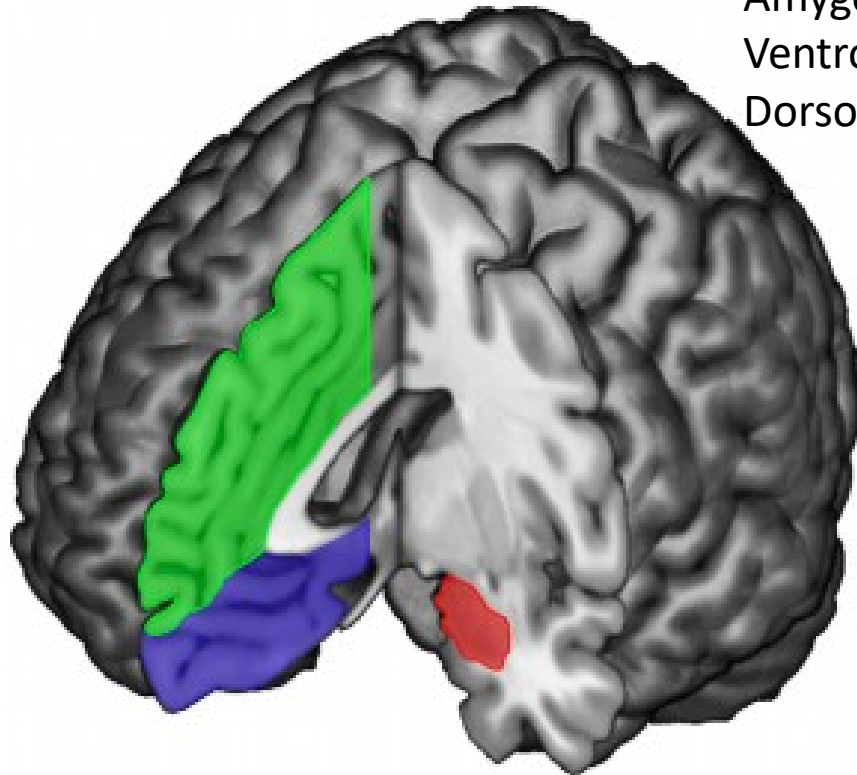
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Disclosures 2019-2020

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- *Research support:* Genentech, Headspace Inc., LundbeckAS, Neurocentria Inc., Pfizer Pharmaceuticals, Roche TCRC Inc., Sunovion Pharmaceuticals Inc., Takeda/Shire Pharmaceuticals Inc., and Tris.
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Amygdala-Prefrontal Circuitry



Amygdala: Red

Ventromedial prefrontal cortex: Blue

Dorsomedial prefrontal cortex: Green

Fig. 1. Structural magnetic resonance image of the human brain highlighting the major components of the amygdala-prefrontal circuitry: amygdala (red), ventromedial prefrontal cortex (blue), and dorsomedial prefrontal cortex (green) (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article).

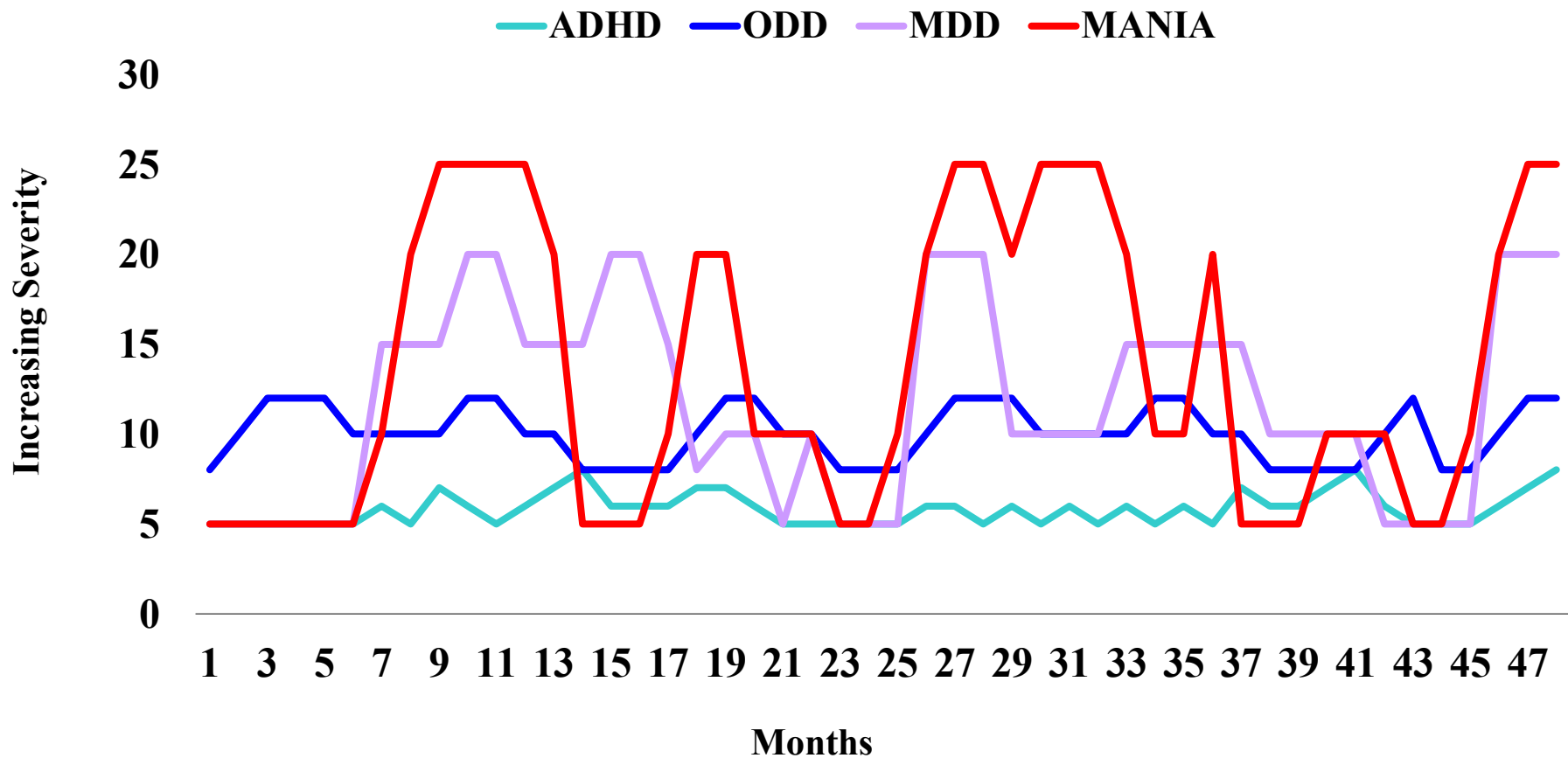
(Kim 2011 Behavioral Brain Research)



Are All Forms of Irritability the Same?

Heterogeneity of Irritability

Heterogeneity of Irritability in Children



Heterogeneity of Irritability

- Labile mood/hot temper: ODD
- Severe irritability: MDD
- Explosive/violent irritability: BPD

Juvenile Mania

- The type of irritability observed in manic children is very severe, persistent, and often violent.
- The outbursts often include threatening or attacking behavior towards others, including family members, other children, adults, and teachers.

Deficits in Emotional Regulation vs. Mood Disorders

- In contrast to mood disorders, subjects with deficits in emotional regulation do not have distinct episodes of DESR
- Unlike mood episodes, deficits in emotional regulation subsides relatively rapidly and does not form a distinct protracted episode of the type that would qualify for a mood disorder
- Thus, subjects with deficits in emotional regulation have normal moods but can become easily frustrated or angry with unexpected emotional challenges

Deficits in Emotional Regulation vs. Mood Disorders: Important Caveat

- **Deficits in emotional regulation and Mood Disorders are not mutually exclusive and can co-exist**



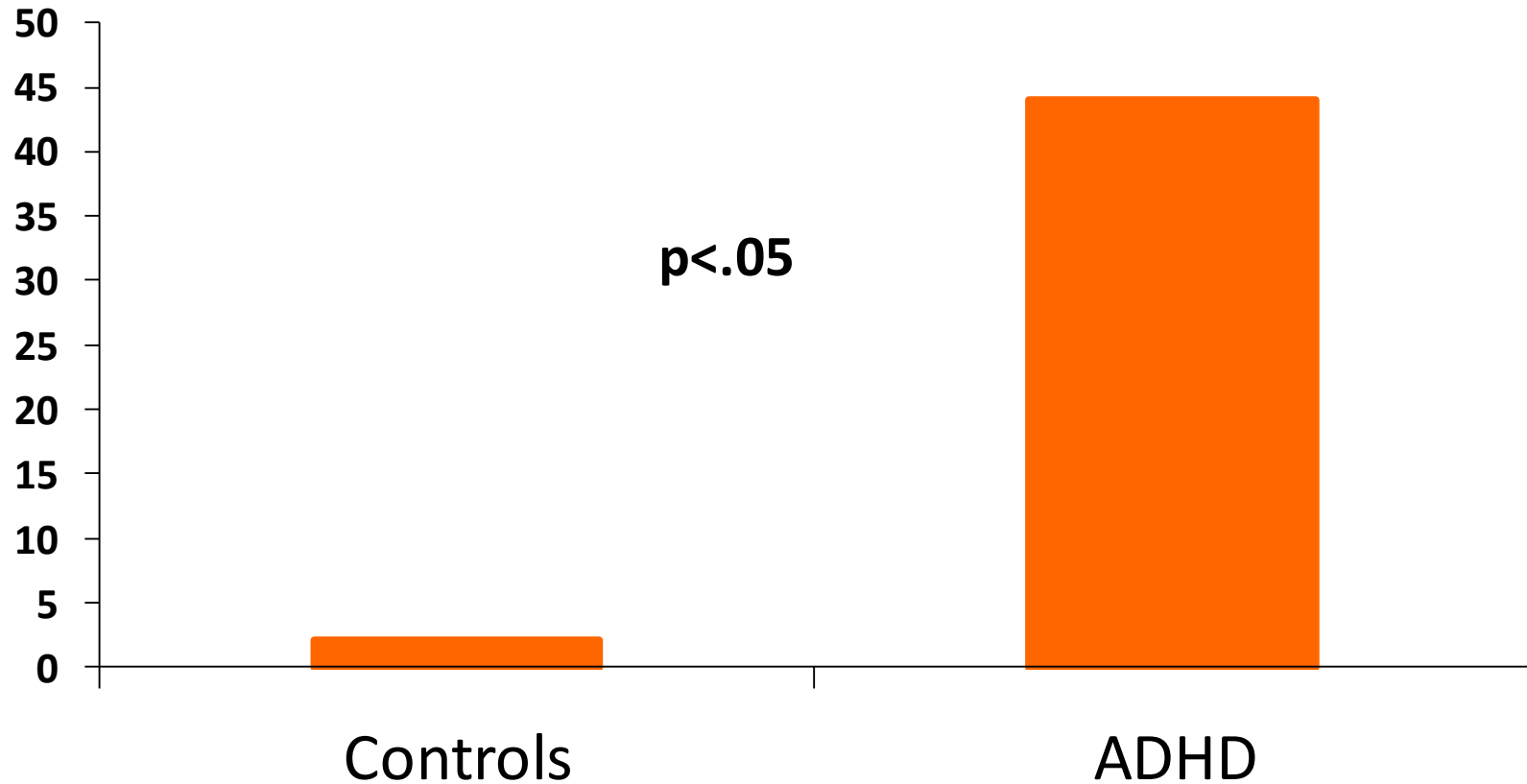
The MGH Study of Deficient Emotional Self Regulation in Pediatric ADHD

CBCL Mood Dysregulation Profiles

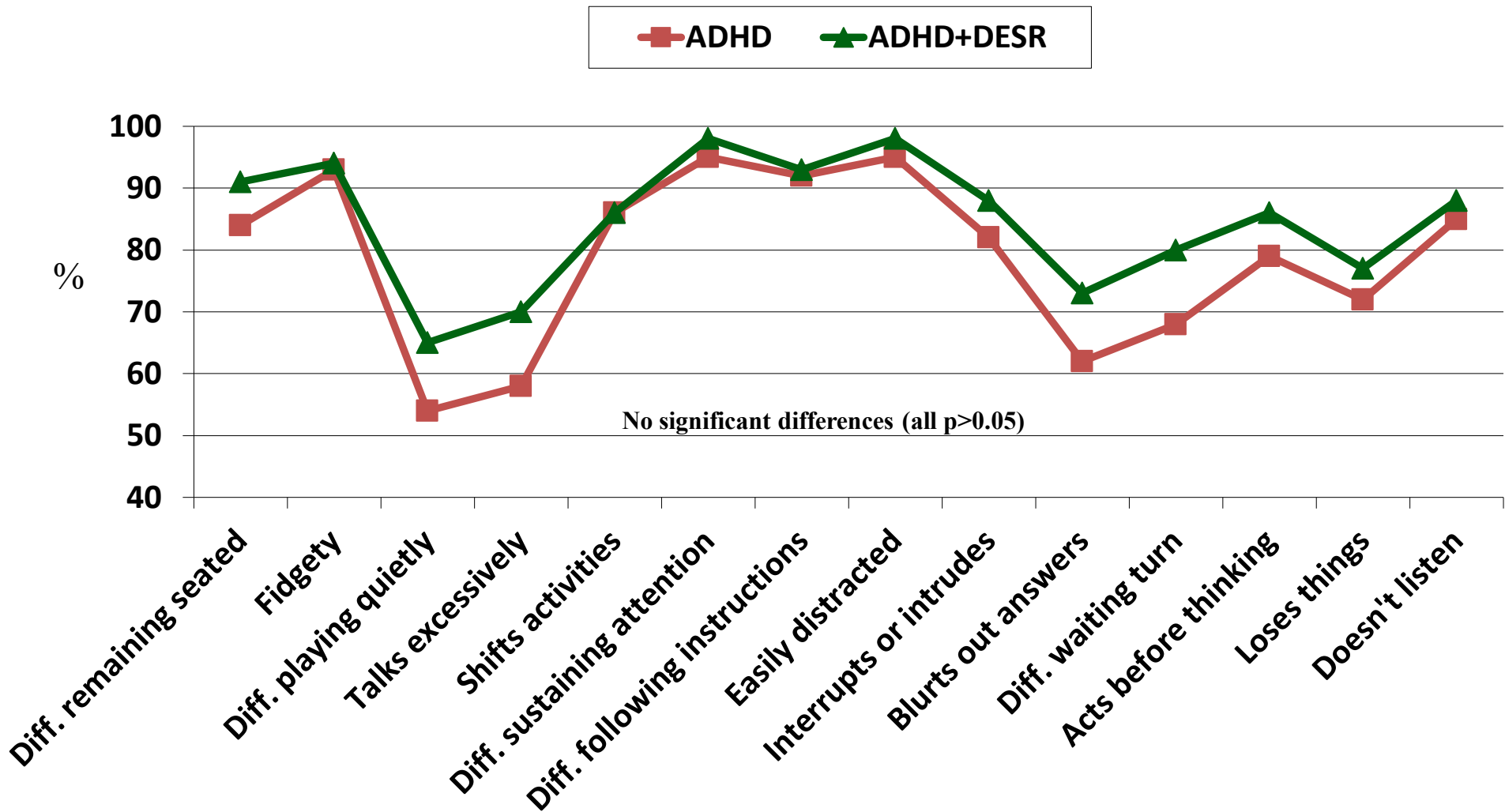
- **CBCL-DESR** was operationalized using an aggregate score ≥ 180 and < 210 in the Anxious/Depressed, Attention, and Aggression scales (AAA profile) of the CBCL
- **CBCL-Severe Dysregulation (BP)** profile was defined as ≥ 210 on the CBCL-AAA scale

Rates of DESR in ADHD and Control Youth

(Spencer et al., Postgrad Med 2012)



ADHD Symptoms



ADHD predicts DESR

Independent of Lifetime History of Comorbidity

(Spencer et al., Postgrad Med 2012)

Regression model included individual comorbid disorders and ADHD as DESR predictors

RED = association with DESR



ADHD remained associated with DESR when covaried with each comorbidity

Oppositional Defiant Disorder
Conduct Disorder
Multiple Anxiety Disorders
Bipolar Disorder
Major Depression
Substance Use Disorders

Main Findings of Pediatric ADHD Study

- 44% of ADHD children had a + CBCL-DESR profile vs. 2% of controls ($p < 0.001$)
- The CBCL-DESR profile was associated with elevated rates of anxiety disorders, CD and ODD but not major depression or bipolar disorder

Severity of the Aggression/Anxiety-Depression/Attention Child Behavior Checklist Profile Discriminates Between Different Levels of Deficits in Emotional Regulation in Youth With Attention-Deficit Hyperactivity Disorder

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Thomas Spencer, MD,*† Stephen V. Faraone, PhD,‡§ Craig B. H. Surman, MD,*†
Janet Wozniak, MD*†

ABSTRACT: *Objective:* We examined whether severity scores (1 SD vs 2 SDs) of a unique profile of the Child Behavior Checklist (CBCL) consisting of the Anxiety/Depression, Aggression, and Attention (AAA) scales would help differentiate levels of deficits in children with attention-deficit hyperactivity disorder (ADHD). *Study Design:* Subjects were 197 children with ADHD and 224 without ADHD. We defined deficient emotional self-regulation (DESR) as an aggregate cutoff score of >180 but <210 (1 SD) on the AAA scales of the CBCL (CBCL-DESR) and Severe Dysregulation as an aggregate cutoff score of ≥ 210 on the same scales (CBCL-Severe Dysregulation). All subjects were assessed with structured diagnostic interviews and a range of functional measures. *Results:* Thirty-six percent of children with ADHD had a positive CBCL-DESR profile versus 2% of controls ($p < .001$) and 19% had a positive CBCL-Severe Dysregulation profile versus 0% of controls ($p < .001$). The subjects positive for the CBCL-Severe Dysregulation profile differed selectively from those with the CBCL-DESR profile in having higher rates of unipolar and bipolar mood disorders, oppositional defiant and conduct disorders, psychiatric hospitalization at both baseline and follow-up assessments, and a higher rate of the CBCL-Severe Dysregulation in siblings. In contrast, the CBCL-DESR was associated with higher rates of comorbid disruptive behavior, anxiety disorders, and impaired interpersonal functioning compared with other ADHD children. *Conclusion:* Severity scores of the AAA CBCL profiles can help distinguish 2 groups of emotional regulation problems in children with ADHD.

(*J Dev Behav Pediatr* 33:236–243, 2012) **Index terms:** affective symptoms, CBCL, bipolar disorder, severity of illness index.



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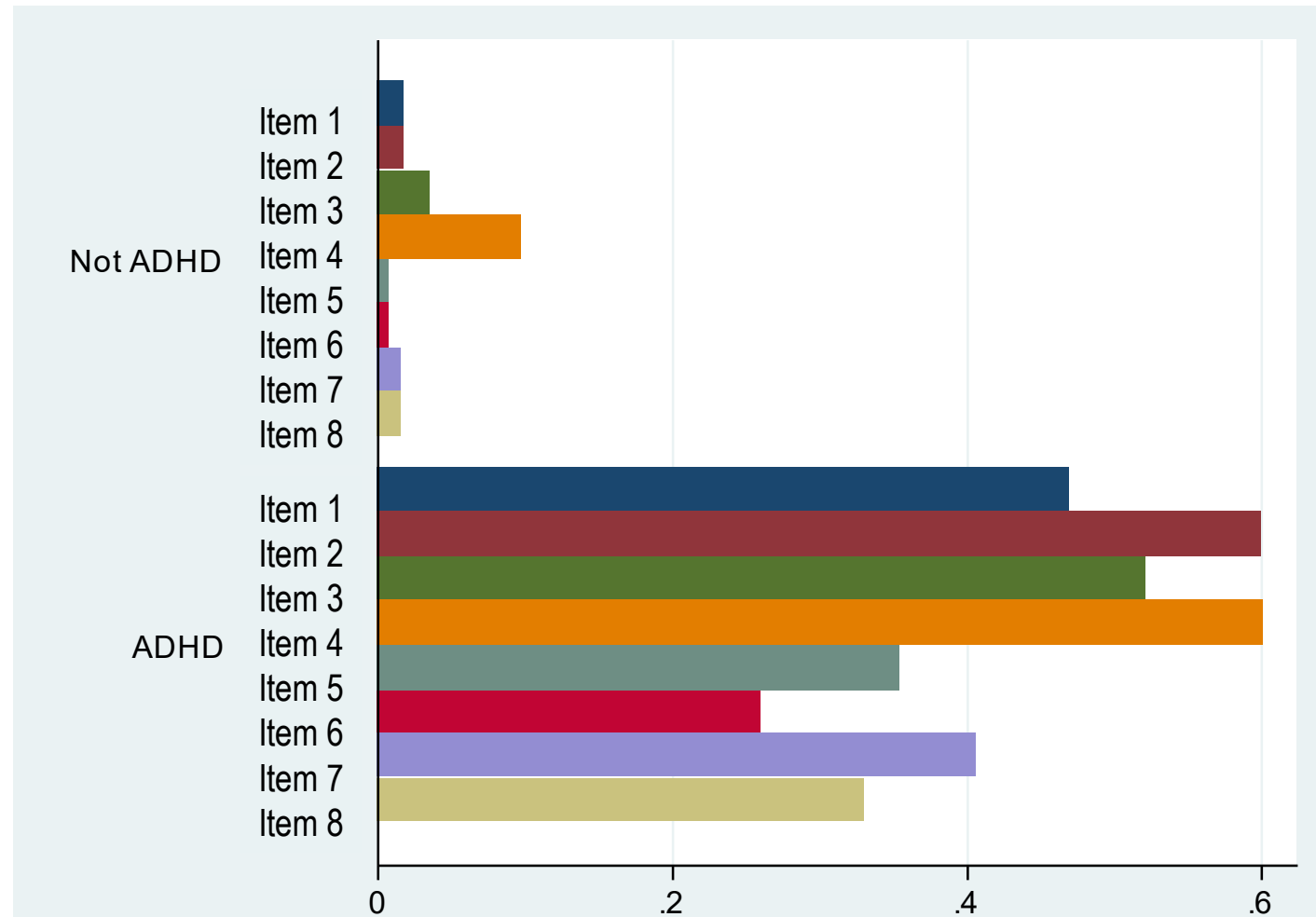
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The MGH Study of Deficient Emotional Self Regulation in Adult ADHD

Deficient Emotional Self Regulation Inventory Items

- 1. Quick to get angry or become upset
 - 2. Easily Frustrated
 - 3. Over-react emotionally
 - 4. Easily excited by activities going on around me
 - 5. Lose my temper
 - 6. Argue with others
 - 7. Am touchy or easily annoyed by others
 - 8. Am angry or resentful
- **Severity: None (0), Sometimes (1) Often (2), Very Often (3)**
- **Items from Barkley's Current Behavior Scale**

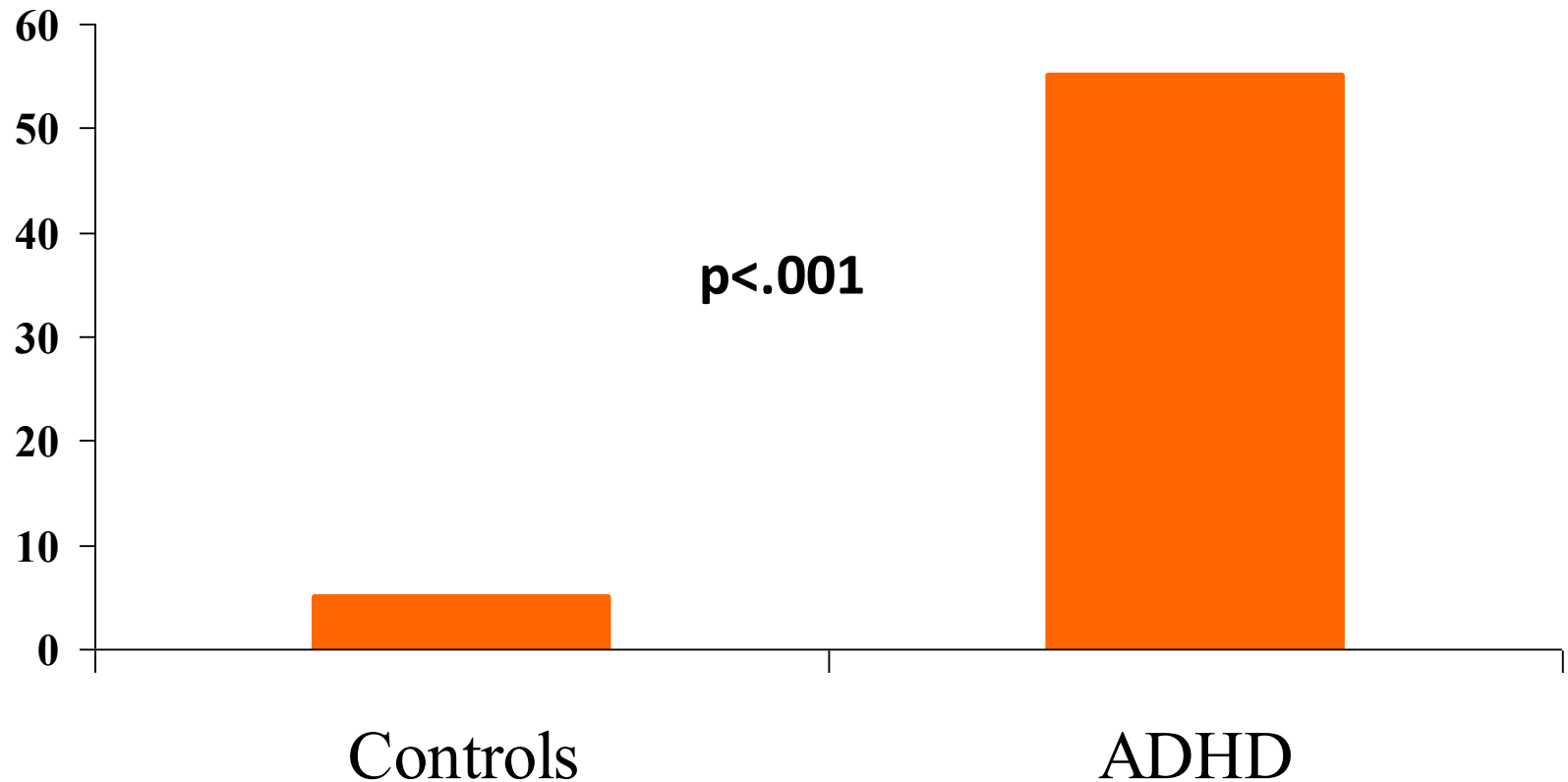
Rate of subjects endorsing DESR symptoms as “Often” or “Very Often”



Internal Consistency of Items (Cronbach's alpha: 0.90)

DESR in ADHD and Control Adults

(Surman et al., American J Psychiatry, 2011)



ADHD predicts DESR Independent of Lifetime and Current Comorbidity

(Surman et al., American J Psychiatry, 2011)

Regression model included individual comorbid disorders and ADHD
as DESR predictors

RED= association with DESR

**ADHD remained associated
with DESR when covaried
with each comorbidity**

Disruptive Behavior Disorders

Major Depression

Anxiety Disorders

Alcohol Abuse

Substance Dependence

Bipolar Disorder

Substance Abuse

Alcohol Dependence

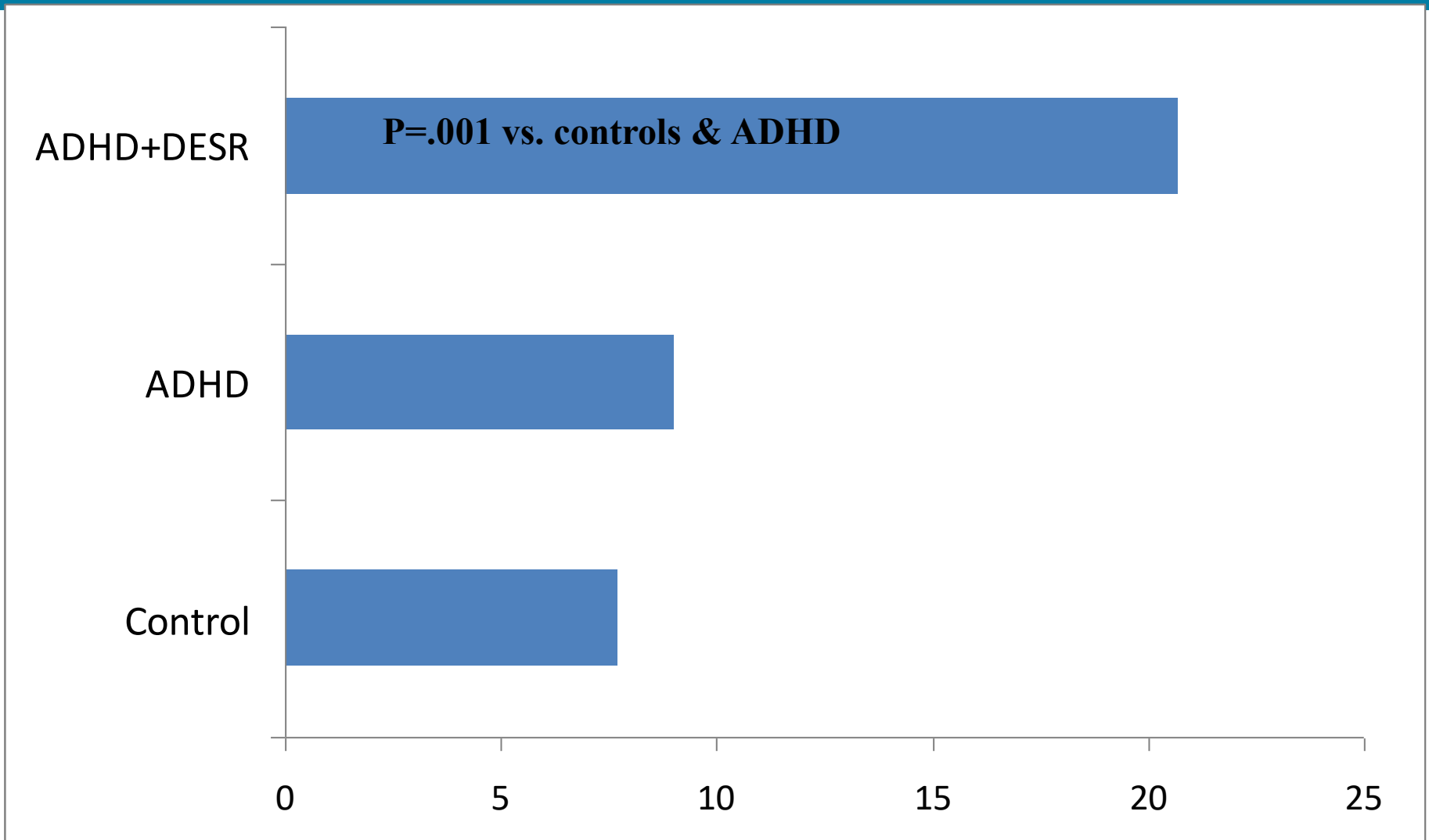
Quality of Life Enjoyment / Satisfaction in ADHD+DESR Probands

	Correlation	z	P
1. Work	-0.32	-3.53	< 0.001
2. Household activities	-0.43	-7.43	< 0.001
3. Social relationships	-0.46	-8.31	< 0.001
4. Family relationships	-0.45	-7.58	< 0.001
5. Leisure time activities	-0.44	-8.22	< 0.001
6. Ability to function in daily life	-0.54	-8.40	< 0.001
7. Sexual drive, interest, and/or performance	-0.43	-7.65	< 0.001
8. Economic status	-0.40	-6.62	< 0.001
9. Living or housing situation	-0.38	-9.08	< 0.001

ADHD/NOS n = 206; Control n =123

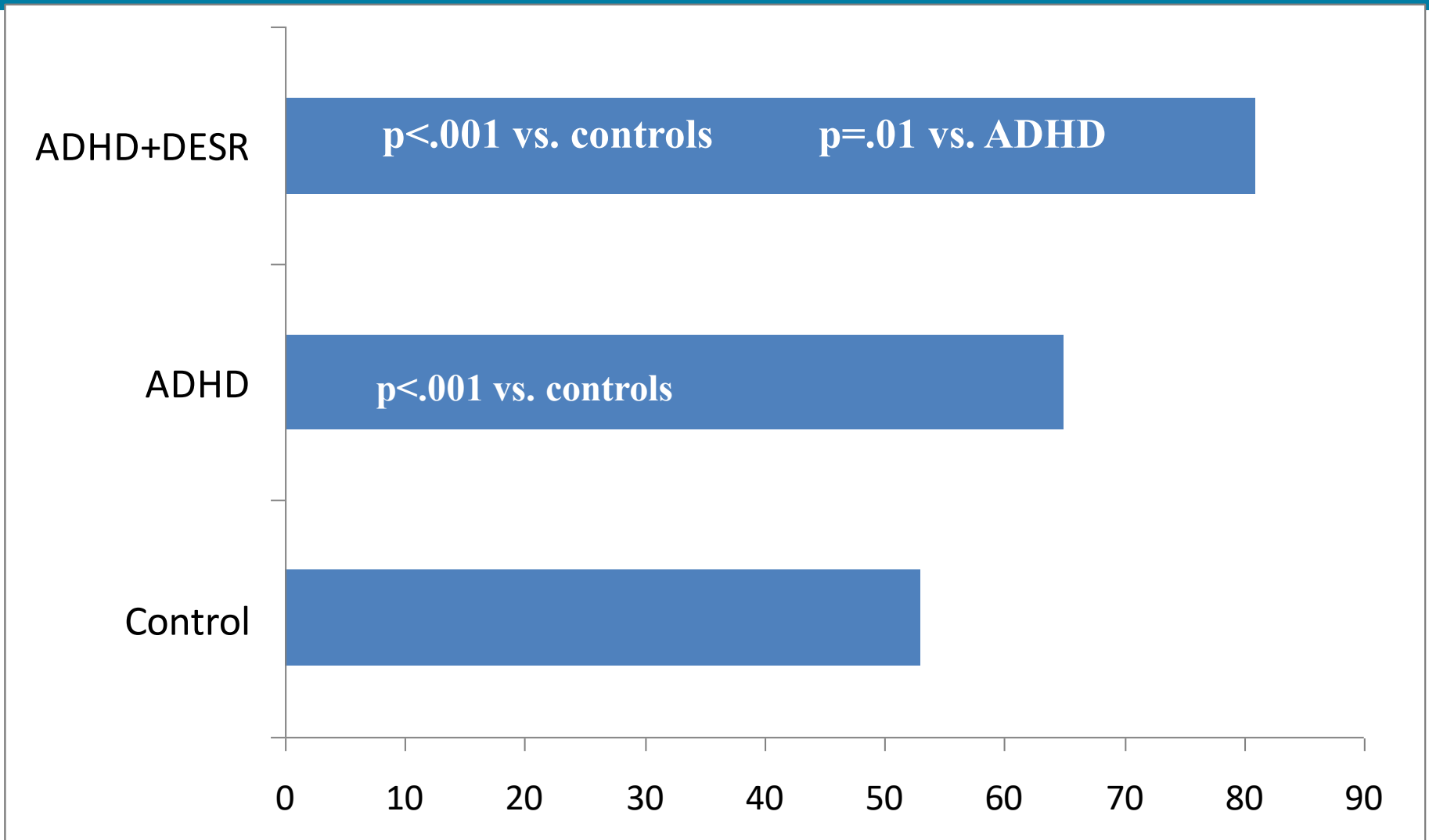
Rates of Divorce by Proband Diagnosis

(Surman et al., American J Psychiatry, 2011)



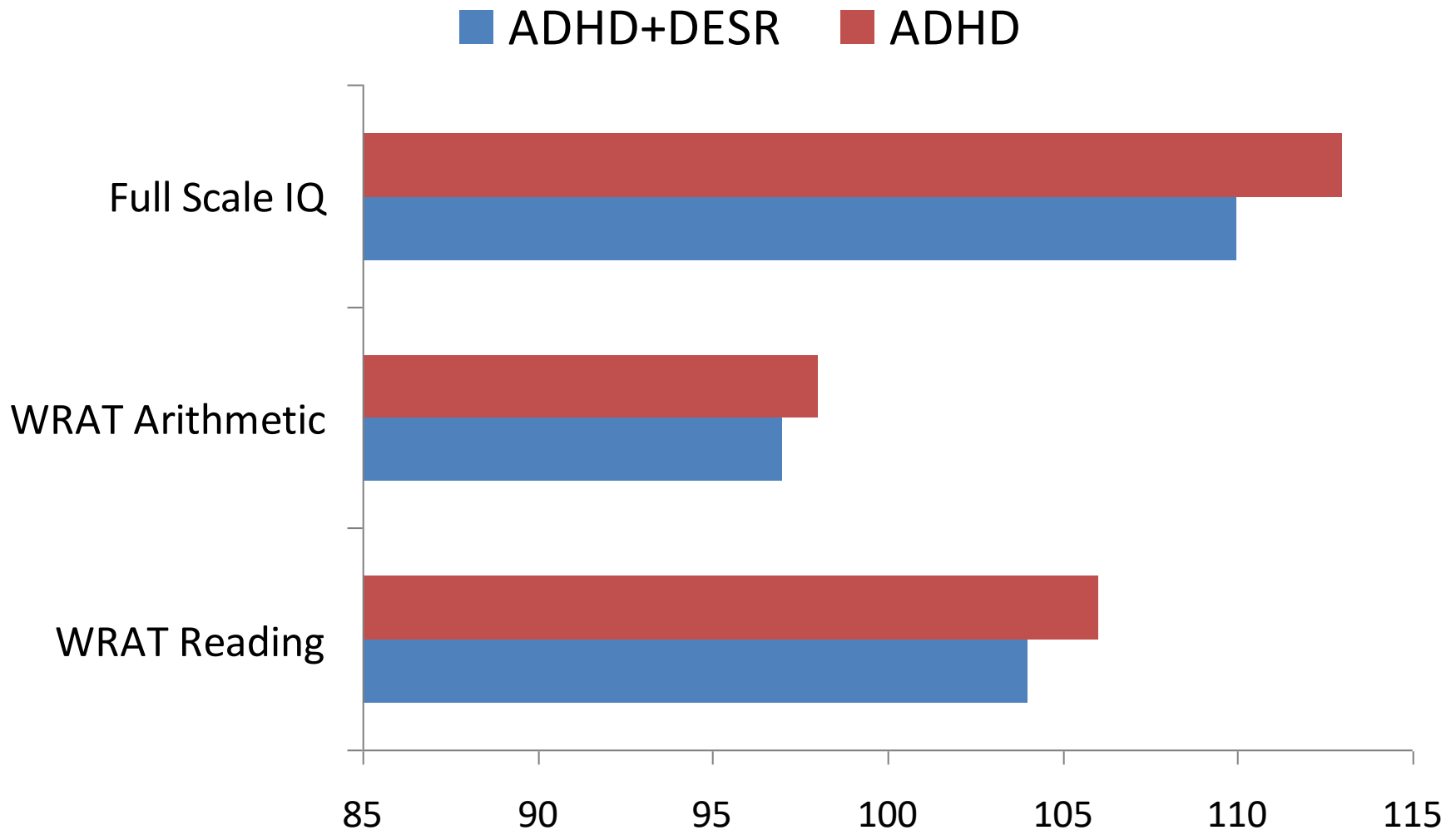
Percent of Subjects who Ever Had an Auto Accident

(Surman et al., American J Psychiatry, 2011)



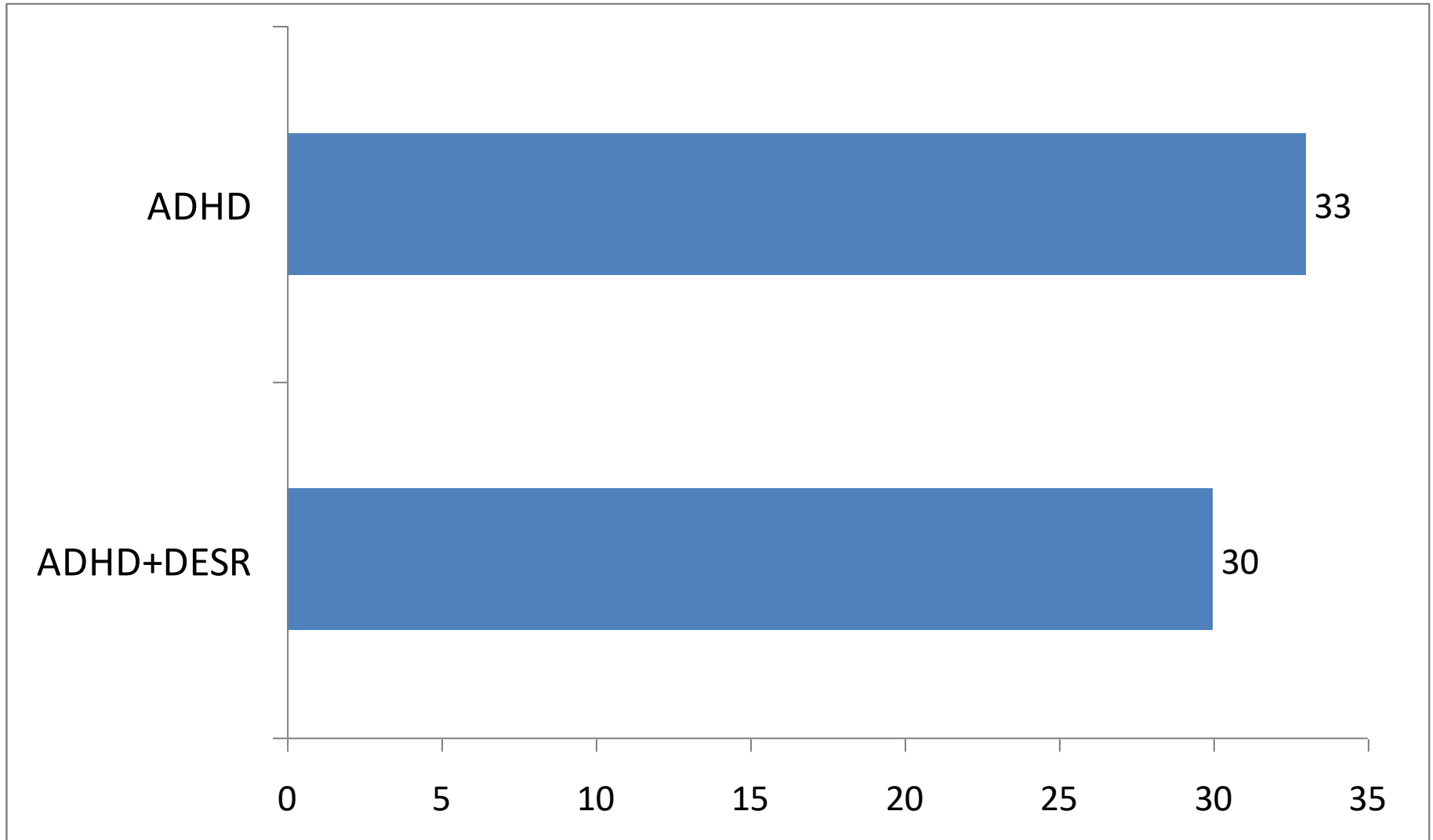
Intellectual Functioning and DESR

(Surman et al., American J Psychiatry, 2011)



Rates of Executive Function Disorder in ADHD Adults With and Without DESR

(Surman et al., American J Psychiatry, 2011)



Summary of DESR Findings in Adults with ADHD

- **A Large Community Sample of Adults with and without ADHD reveals:**
- **DESR questionnaire validity**
 - Acceptable internal consistency
 - Correlated with functional impairment
- **A sizeable majority of ADHD Adults had DESR**
- **Comorbidity did not account for DESR in ADHD adults**

Article

Deficient Emotional Self-Regulation and Adult Attention Deficit Hyperactivity Disorder: A Family Risk Analysis

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Objective: A growing body of research suggests that deficient emotional self-regulation (DESR) is prevalent and morbid among patients with attention deficit hyperactivity disorder (ADHD). Family studies provide a method of clarifying the co-occurrence of clinical features, but no family studies have yet addressed ADHD and DESR.

Method: Participants were 83 probands with and without ADHD and 128 siblings. All were assessed for axis I DSM-IV conditions with structured diagnostic interviews. The authors defined DESR in adult probands and siblings using items from the Barkley Current Behavior Scale. Analyses tested hypotheses about the familial relationship between ADHD and DESR.

Results: Siblings of ADHD probands were at elevated risk of having ADHD, irrespective of the presence or absence of DESR in the proband. The risk for DESR was

elevated in siblings of ADHD plus DESR probands but not in siblings of ADHD probands. ADHD and DESR cosegregated in siblings. The risk for other psychiatric disorders was similar in siblings of the ADHD proband groups.

Conclusions: The pattern of inheritance of ADHD with DESR preliminarily suggests that DESR may be a familial subtype of ADHD. Our data suggest that DESR is not an expression of other axis I DSM-IV disorders or of nonfamilial environmental factors. The authors cannot exclude contribution of non-axis-I DSM-IV disorders to risk for DESR and cannot determine whether the cosegregation of ADHD in DESR within families is a result of genes or familial environmental risk factors. Further investigation of DESR and its correlates and treatment both in and outside the context of ADHD is warranted.

(*Am J Psychiatry* Surman et al.; *AiA*:1–7)

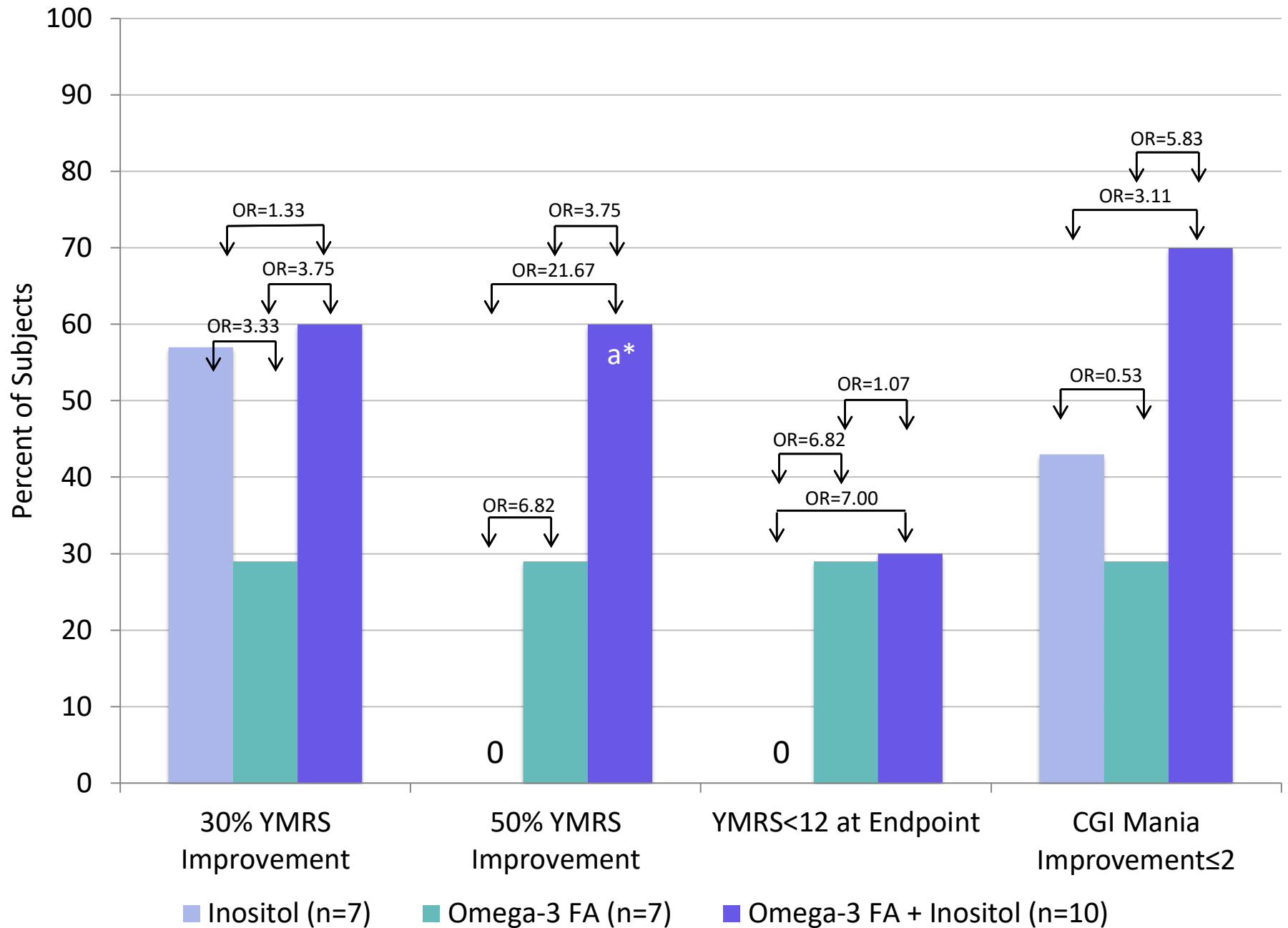


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Therapeutic Opportunities

HIGH EPA OMEGA-3 FATTY ACIDS AND INSOSITOL IN PEDIATRIC BPD STUDY: ANTIMANIC RESPONSE



Summary

- Deficits in emotional regulation are frequently associated with ADHD and ASD in both children and adults
- Deficits in emotional regulation increase the risk for mood disorders and associated conditions
- Deficits in emotional regulation are associated with functional impairment in both pediatric and adult patients with ADHD and ASD
- Deficits in emotional regulation are independent of psychiatric comorbidity