Mood disorders in child psychiatry

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Forensic Psychiatrist
Associate Professor
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Potential conflict of interest

- Consultant et speaker:
  - Janssen
  - Shire
  - Purdue

Emotional Dysregulation

An inability to modulate emotional responses, resulting in extreme responses of an internalizing or externalizing nature that would be considered inappropriate for the developmental age of the person

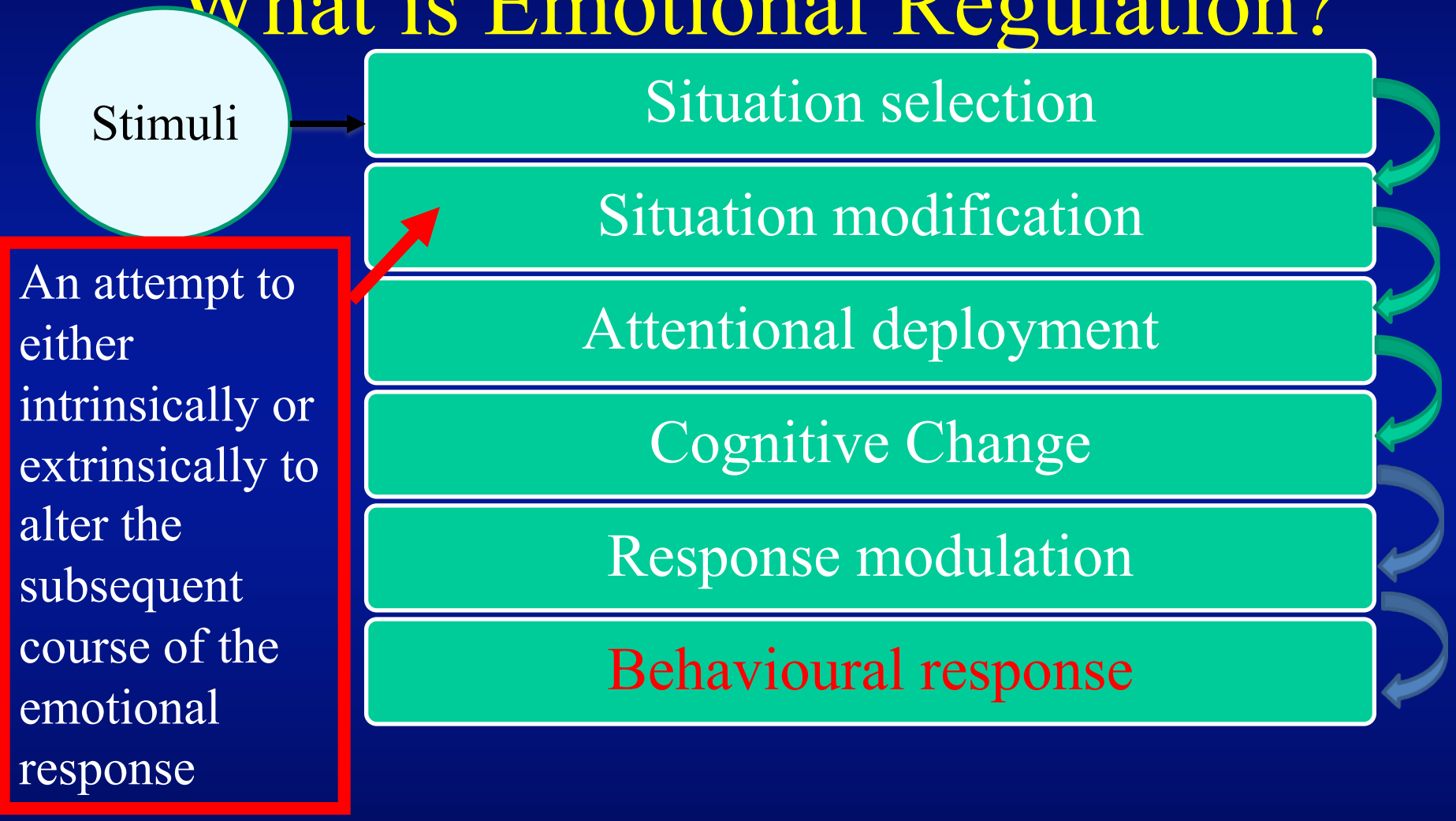
van Stralen, 2016

What is Emotion?

- Change in intentional state
- Short duration
  - Subjective component - how we experience the emotion
  - Physiological component - how our bodies react to the emotion
  - Expressive component - how we behave in response to the emotion

Hess, H. & Thibault, P. (2009). Darwin and emotion expression. *American Psychologist, 64(2)*, 120-128
Neese, R. & Ellsworth, P. (2009). Evolution, emotions, and emotional disorders. *American Psychologist, 64(2)*, 129-139.

What is Emotional Regulation?



Koole, S. L. et al. (2010). *Handbook of Self-Regulation (2nd Ed.) (pp. 22-40)*. New York: Guilford.
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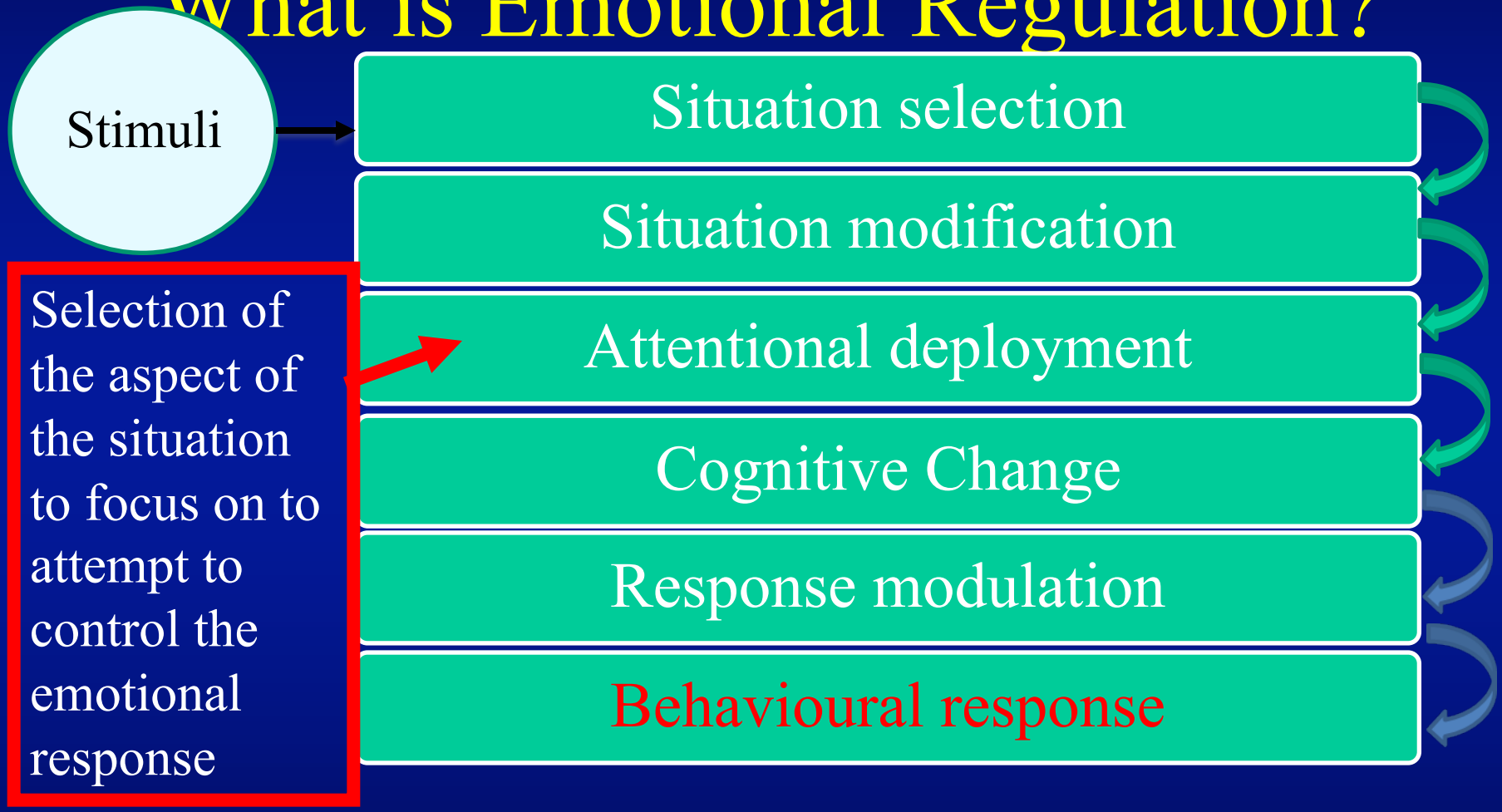

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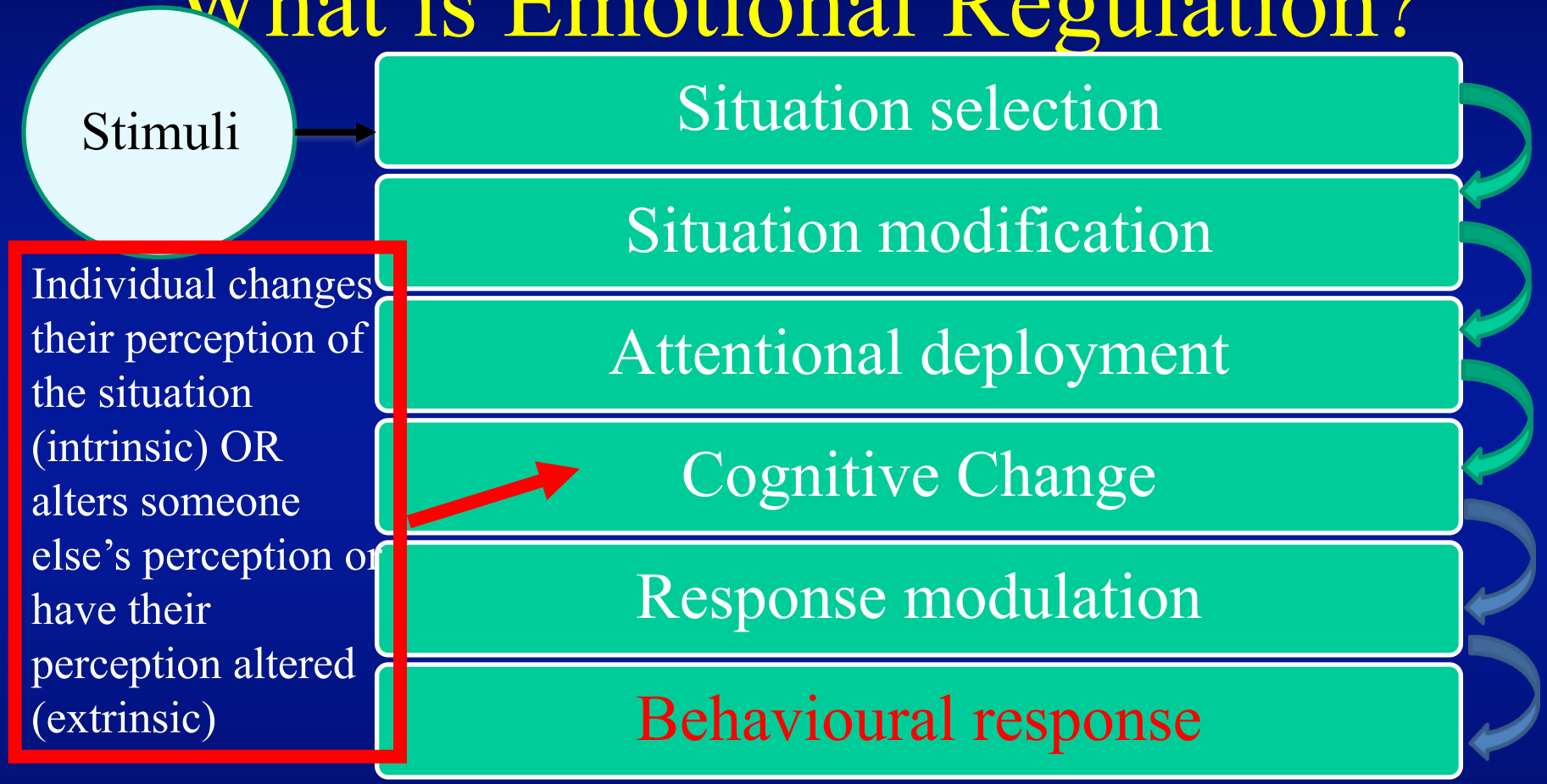

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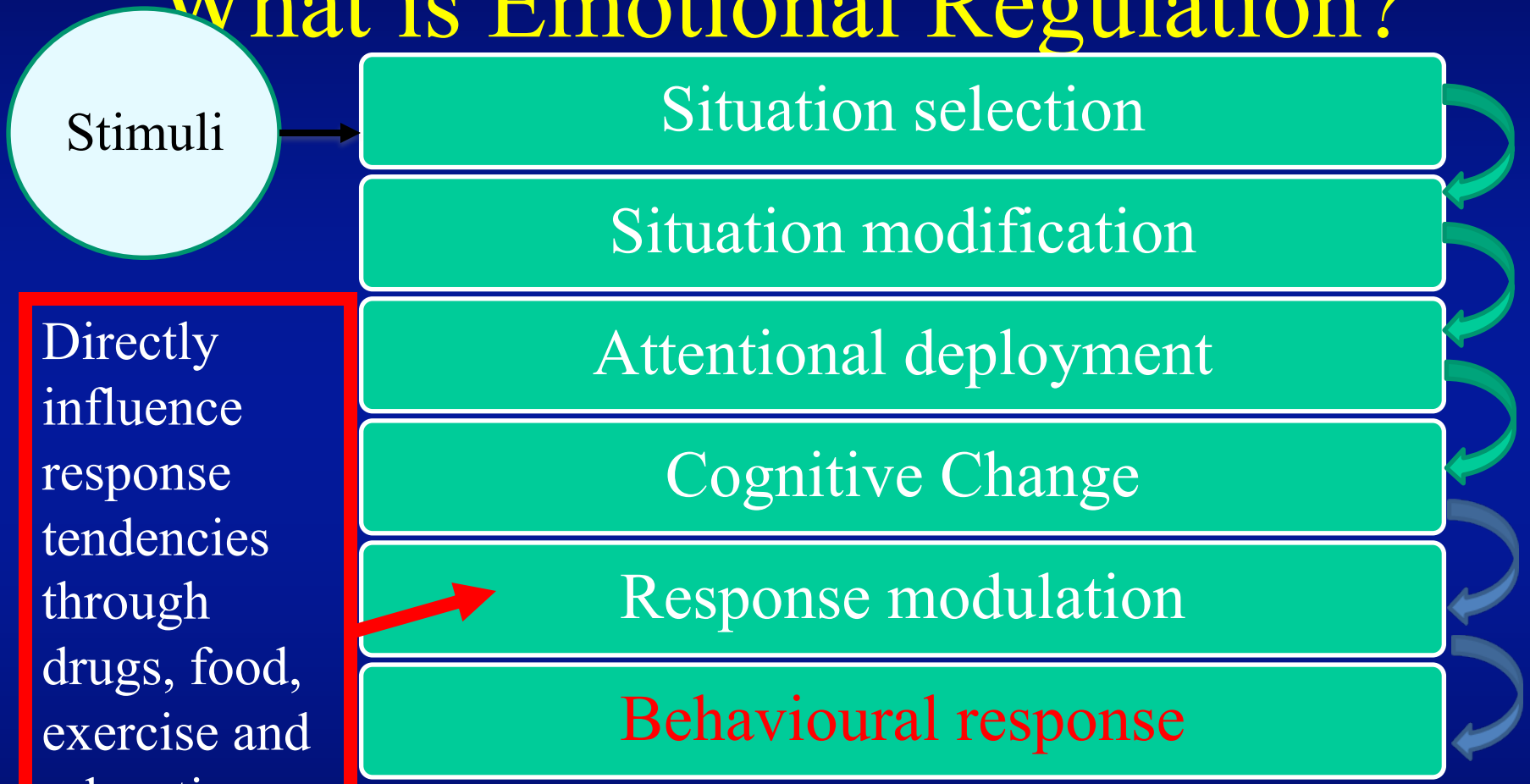

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Gross, J. J. (1998). *Review of General Psychology, 2*, 271-299.
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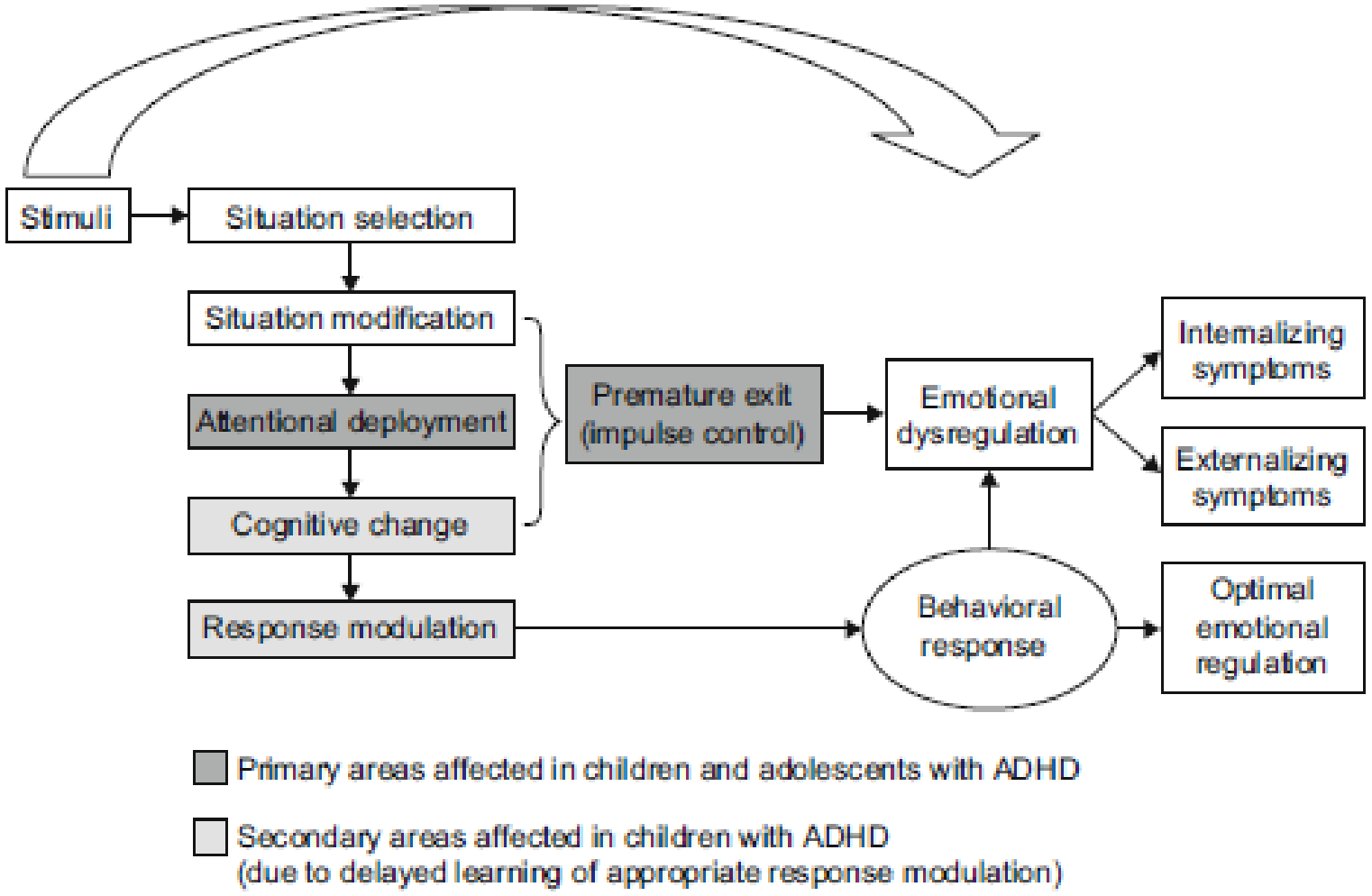
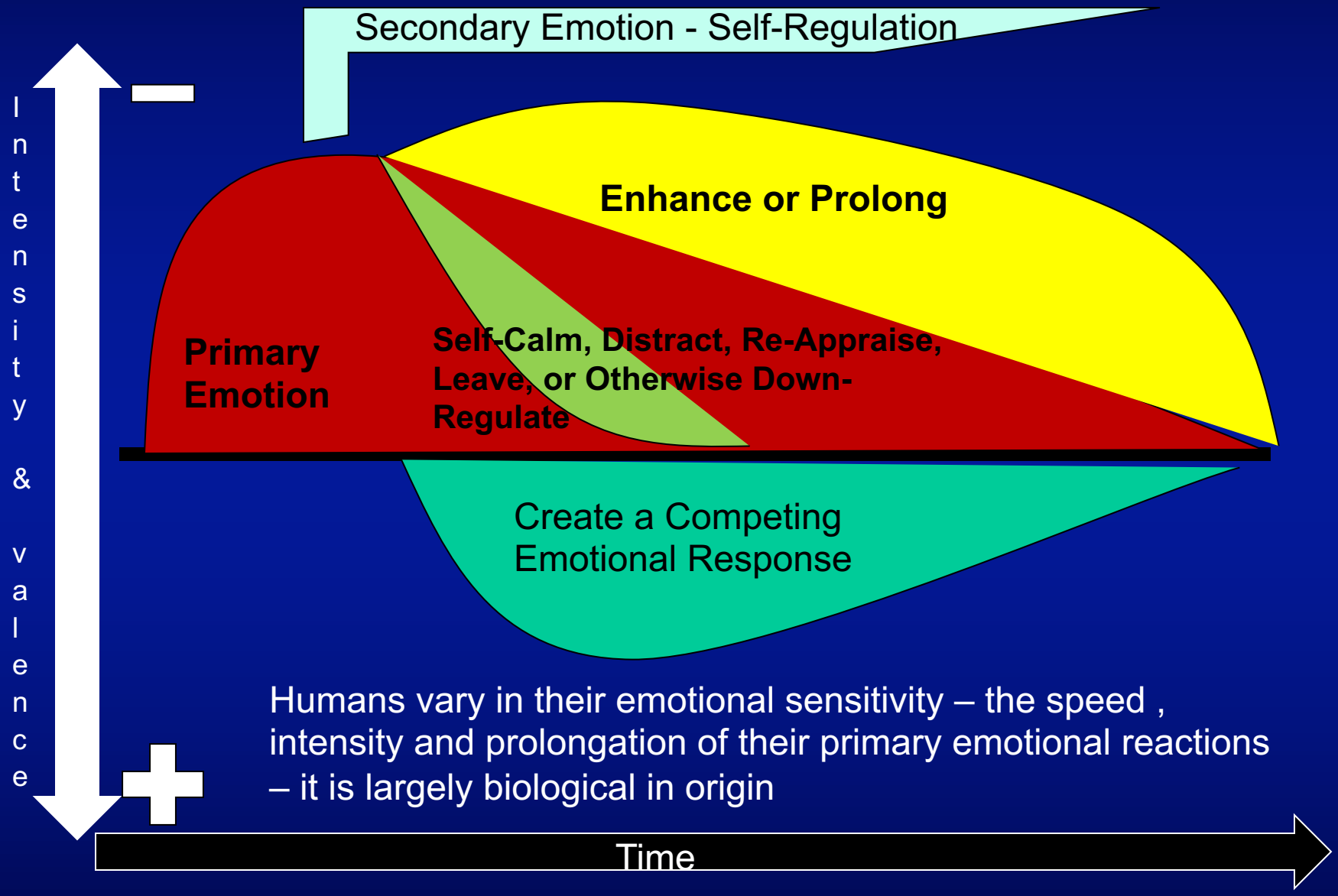
Conceptual Model for Emotional Dysregulation in Children



vanStralen, ADHD Attent Def Hyp Disord, 2016

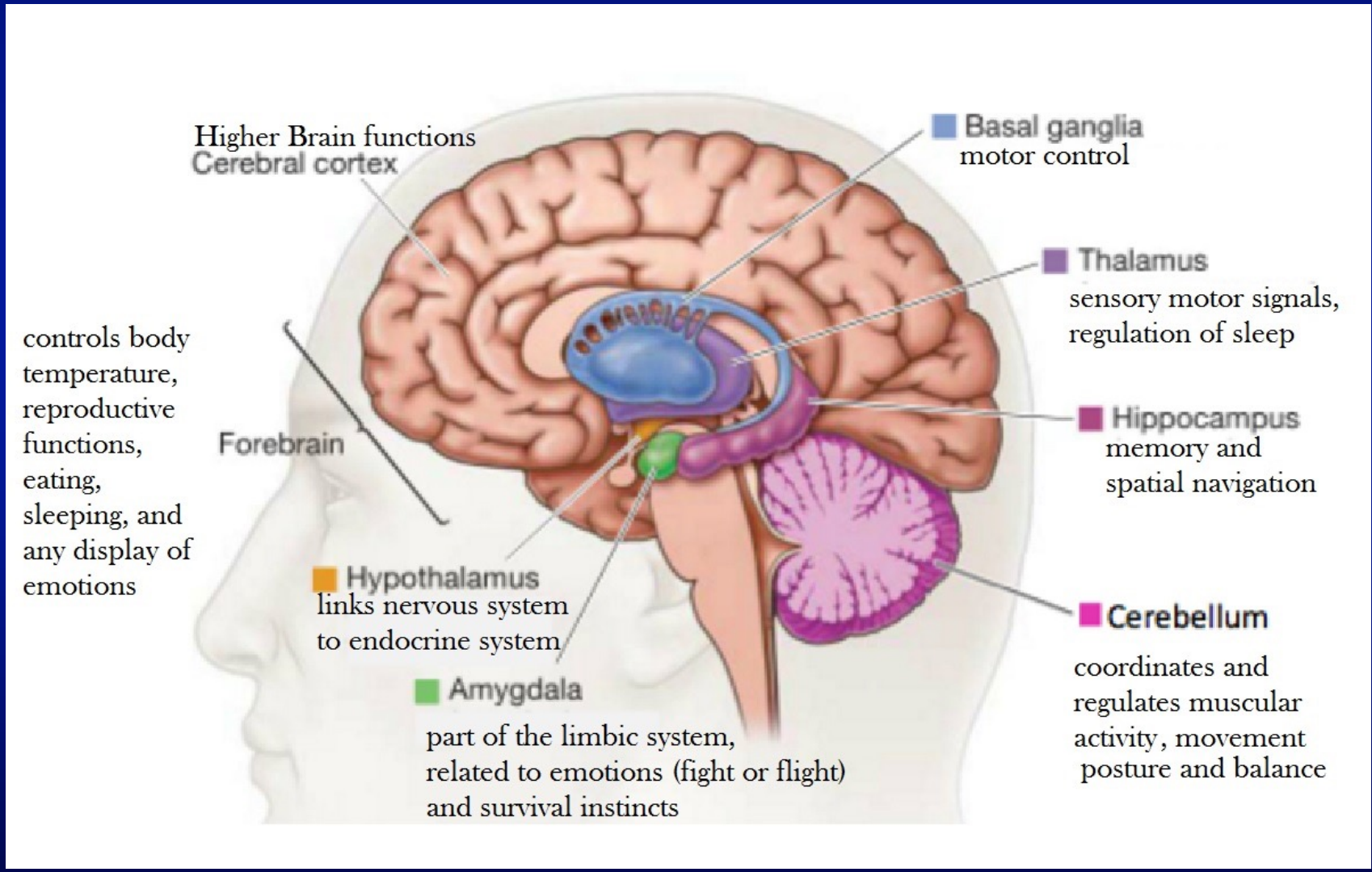
Two Stage Model of Human Emotion



Humans vary in their emotional sensitivity – the speed , intensity and prolongation of their primary emotional reactions – it is largely biological in origin

Adapted from Figure 2.1, Koole, S. L. et al. (2011). The self-regulation of emotion. In K. Vohs & R. Baumeister (Eds.), *Handbook of Self-Regulation (2nd ed.)* (pp. 22-40). New York: Guilford Press.

Amygdala is implicated in the regulation of emotion



DSM-5 Proposed Subcategory Changes for ODD

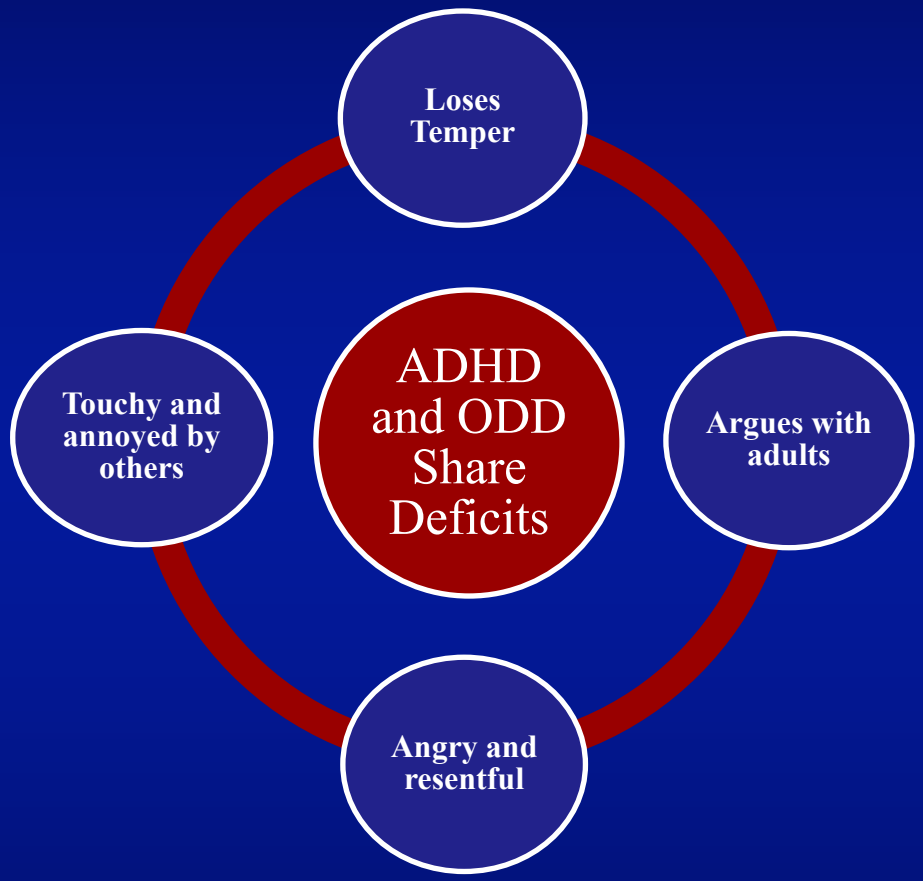
- Angry/Irritable Mood
  - Loses temper
  - Is touchy or easily annoyed by others
  - Is angry and resentful
  - Argues with adults

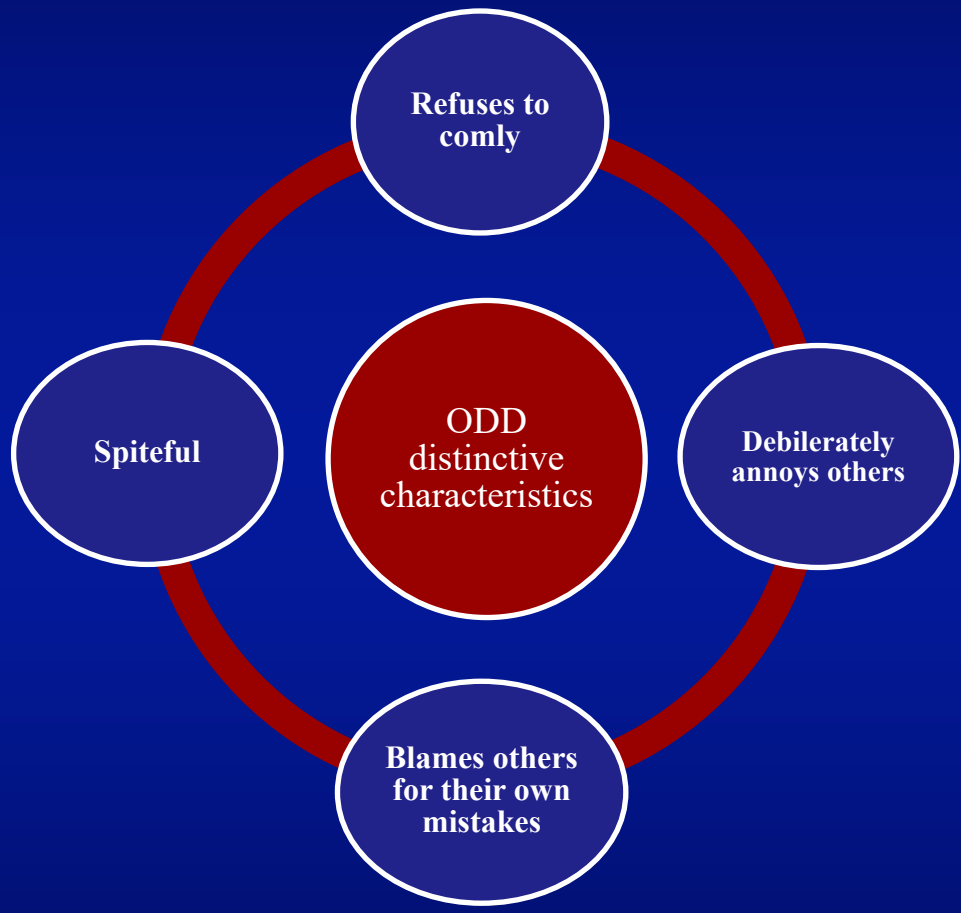
DSM-5 Proposed Subcategory Changes for ODD

- Defiant/headstrong Behaviour
  - Actively defies or refuses to comply with adults' request or rules
  - Deliberately annoys people
  - Blames others for his or her mistakes or misbehaviour
- Vindictiveness
  - Has been spiteful or vindictive at least twice within the past six months

American Psychiatric Association. DSM-V Development. http://www.dsm5.org.

Features of ADHD and ODD





Conduct Disorder

- Heterogeneous manifestations
- Etiologies for disruptive conduct disorder:
  - Inattention, hyperactivity, impulsiveness
  - Mood disorder (dysphoria, mania)
  - Drug addiction
  - Brain damage and epilepsy
  - Psychosis, dissociation
  - Emotional, sexual, physical abuse

DSM-5 Criteria for Conduct Disorder

- Essential characteristic of conduct disorders is repetitive and persistent behaviour manifested by:
  - Violation of others' basic rights or
  - Violation of societal norms or rules (generally age-appropriate)
- At least 3 DSM-5 symptoms during the last 12 months
- At least one symptom present during the last 6 months
- 15 criteria:
  - Aggression to people and animals (7)
  - Destruction of property (2)
  - Deceitfulness or theft (3)
  - Violation of rules (3)

American Psychiatric Association . DSM-5. 2013.

Conduct Disorder: Hypothesis

- Psychopathic traits:
  - Socialized type, Calleous-unemotional, Covert type Delinquant type, Cold profile

- Psychiatric traits
  - Undersocialized type, Impulse-control, Overt type, Aggressive type, Hot profile

  - ADHD: well studied, highly associated with CD
  - Substance Use Disorder: highly prevalent, highly predictive
  - Bipolar Disorder (BPD): controversial

Conduct Disorder

- Limited prosocial emotions (insensitive; impassive)
- Predictor of violence
- Stability of traits
- Poor response to parenting interventions
- Favorable response to psychostimulants

4 domains

1) Absence of guilt
2) Lack of empathy
3) Few concerned with performance
4) Superficial affect

DSM-5 Criteria for Disruptive Mood Dysregulation Disorder

A. Severe recurrent temper outbursts manifested verbally (e.g. verbal rages) and/or behaviourally (e.g., physical aggression toward people or property) that are grossly out of proportion in intensity or duration to the situation or provocation

B. The temper outbursts are inconsistent with developmental level

C. The temper outbursts occur, on average, 3 or more times per week

D. The mood between temper outbursts is persistently irritable or angry most of the day, nearly every day, and is observable by others (e.g., parents, teachers, peers)

American Psychiatric Association DSM-5. 2013.

DSM-5 Criteria for Disruptive Mood Dysregulation Disorder

- Criteria A-D have been persistent for 12 or more months. Throughout that time, the individual has not had a period lasting 3 or more consecutive months without all of the symptoms in criteria A-D.

- Criteria A and D are present in at least 2 of 3 settings (i.e., at home, at school, with peers) and are severe in at least 1 of the 3.

- The diagnosis should not be made for the first time before age 6 or after age 18 years.

American Psychiatric Association DSM-5. 2013.


AUGUST 19, 2002
TIME
THE SKINNY ON THE ANTI-FAT HORMONE
Inside the Volatile World of the
YOUNG AND BIPOLAR
Why are so many kids being diagnosed with the disorder once known as MANIC DEPRESSION?
Ian Palmer, 9, is being treated for bipolar disorder

Major Depressive Episode: Diagnosis

Five or more of the following symptoms are present most of the day, nearly every day, during a period of at least 2 consecutive weeks

1. Depressed mood
2. Loss of interest or pleasure in all/almost all usual activities
3. Significant weight loss or weight gain
4. Insomnia or hypersomnia
5. Psychomotor agitation or retardation
6. Fatigue or loss of energy
7. Diminished ability to think or concentrate or indecisiveness
8. Recurrent thoughts of death or suicide

At least 1 of these 2 symptoms

At least 5 of these 9 total symptoms

Symptoms must cause clinically significant distress or impairment in social, occupational, or other important areas of functioning

Every day, and all day

For at least 2 consecutive weeks

DSM-IV-TR™2000.

Major Depressive Disorder: Diagnosis

a) Presence of a single major depressive episode

b) The major depressive episode is not better accounted for by schizoaffective disorder and is not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder not otherwise specified

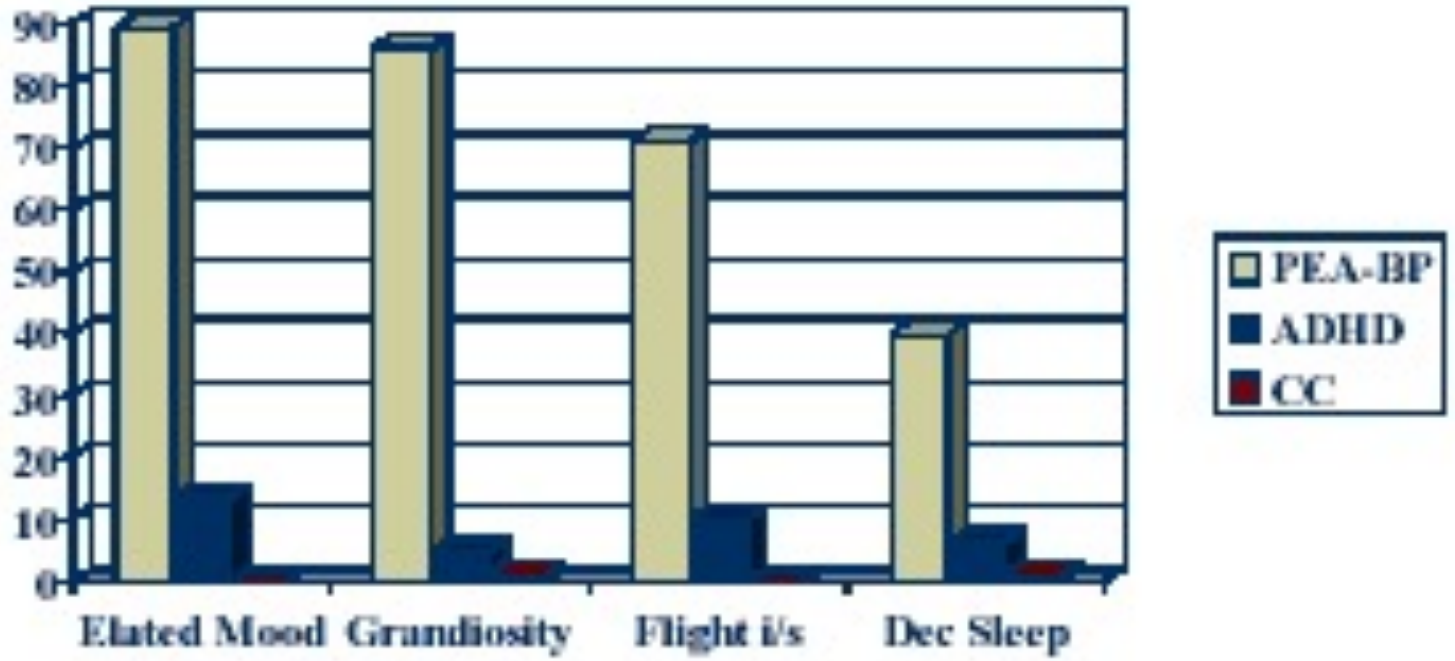
c) There has never been a manic episode, a mixed ep

If Recurrent, the major depressive episodes must be separated by at least 2 months

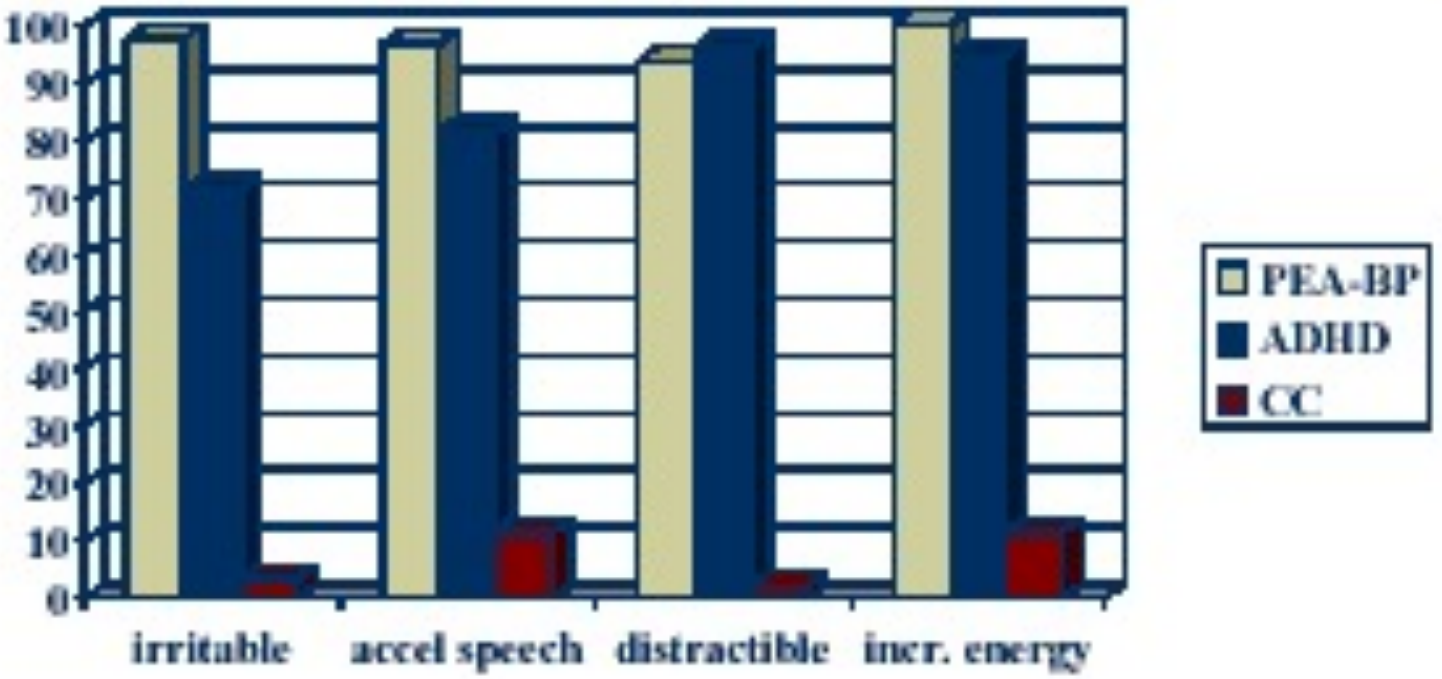
DSM-IV-TR™2000.

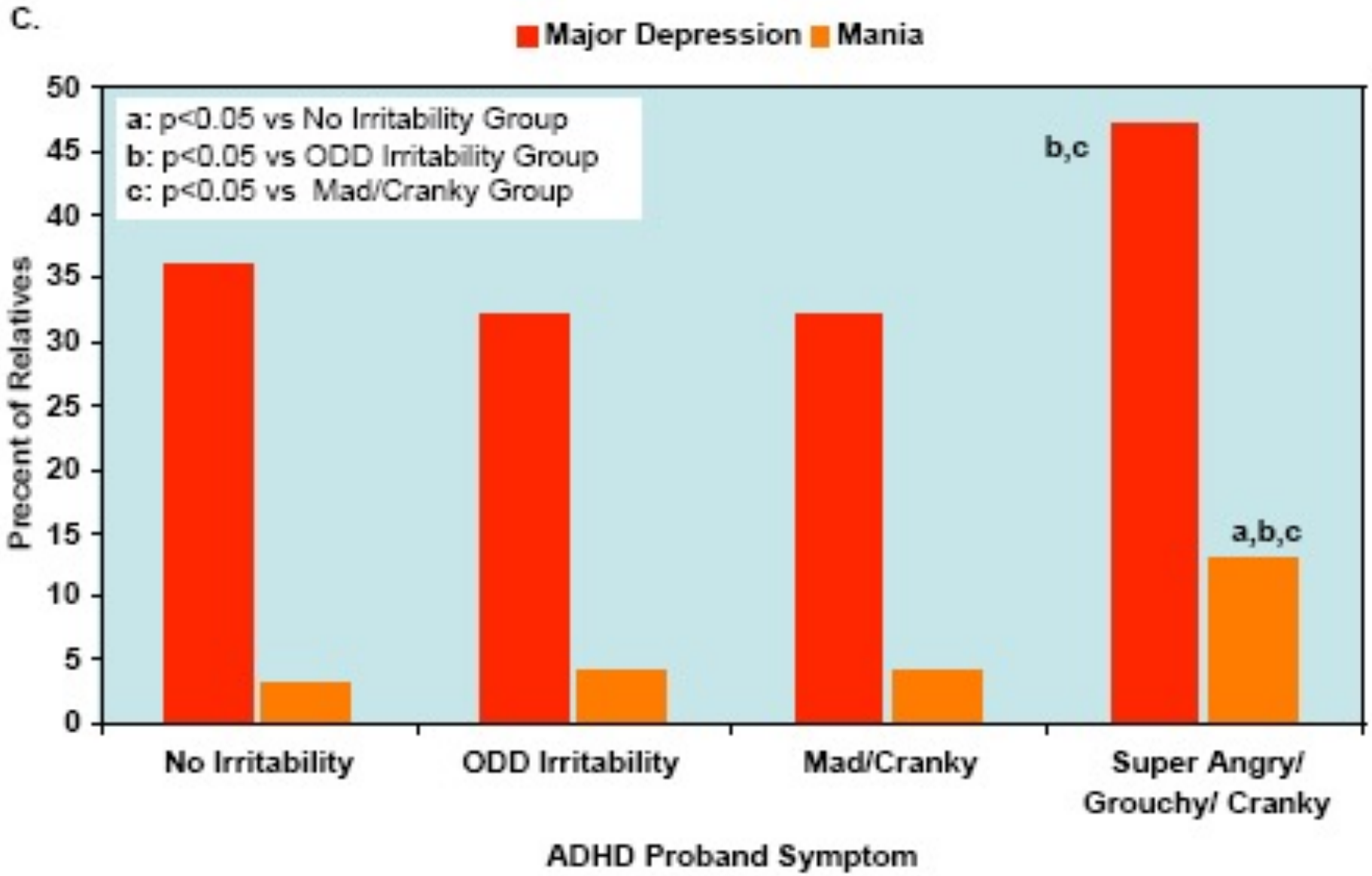
	COBY (Birmaher)		SCMI-P (Carlson)	
Age onset	<12	13-17	15-29	>30
BPI	29,6%	57%	45%	74%
ADHD	82%	66%	26%	8%
Hospit	58%	80%	100%	100%
EGF	36	32	27	28
EGF>70 @ 6mois	9%	18%	58%	55%
Remission@6mois	41%	56%	62%	83%

Mania Specific Symptoms



Non-specific Symptoms





Mick, Biederman, Wozniak; NIMH Ped Bipolar Conf., April 2005

Adult Outcomes of Youth Irritability: A 20-Year Prospective Community-Based Study

Argyris Stringaris, M.D., M.R.C.Psych., Patricia Cohen, Ph.D., Daniel S. Pine, M.D., and Ellen Leibenluft, M.D.

TABLE 2. Irritability in Early Adolescence as Predictor of Disorders at 20-Year Follow-Up[a]

	Adjustment for Disorders in Early Adolescence					
	Not Adjusted		Emotional Disorders		Emotional and Behavioral Disorders	
Disorder in Adulthood	Odds Ratio	95% CI	Odds Ratio	95% CI	Odds Ratio	95% CI
Major depressive disorder	1.48***	1.16–1.89	1.41*	1.08–1.84	1.33*	1.00–1.78
Generalized anxiety disorder	2.11***	1.37–3.24	1.93**	1.19–3.13	1.72*	1.04–2.87
Dysthymia	2.07***	1.34–3.20	2.07**	1.32–3.26	1.81**	1.06–3.12
Bipolar disorder	1.31	0.77–2.24	1.18	0.57–2.44	1.02	0.39–2.69
Axis II disorders	1.03	0.81–1.31	0.97	0.81–1.26	0.85	0.63–1.15

[a] All logistic regression models report unit-based increases in irritability associated with increases in the odds of disorder in adulthood, adjusted for age, sex, and family socioeconomic status. Imputed N=776.

*p<0.05; **p<0.01; ***p<0.001.

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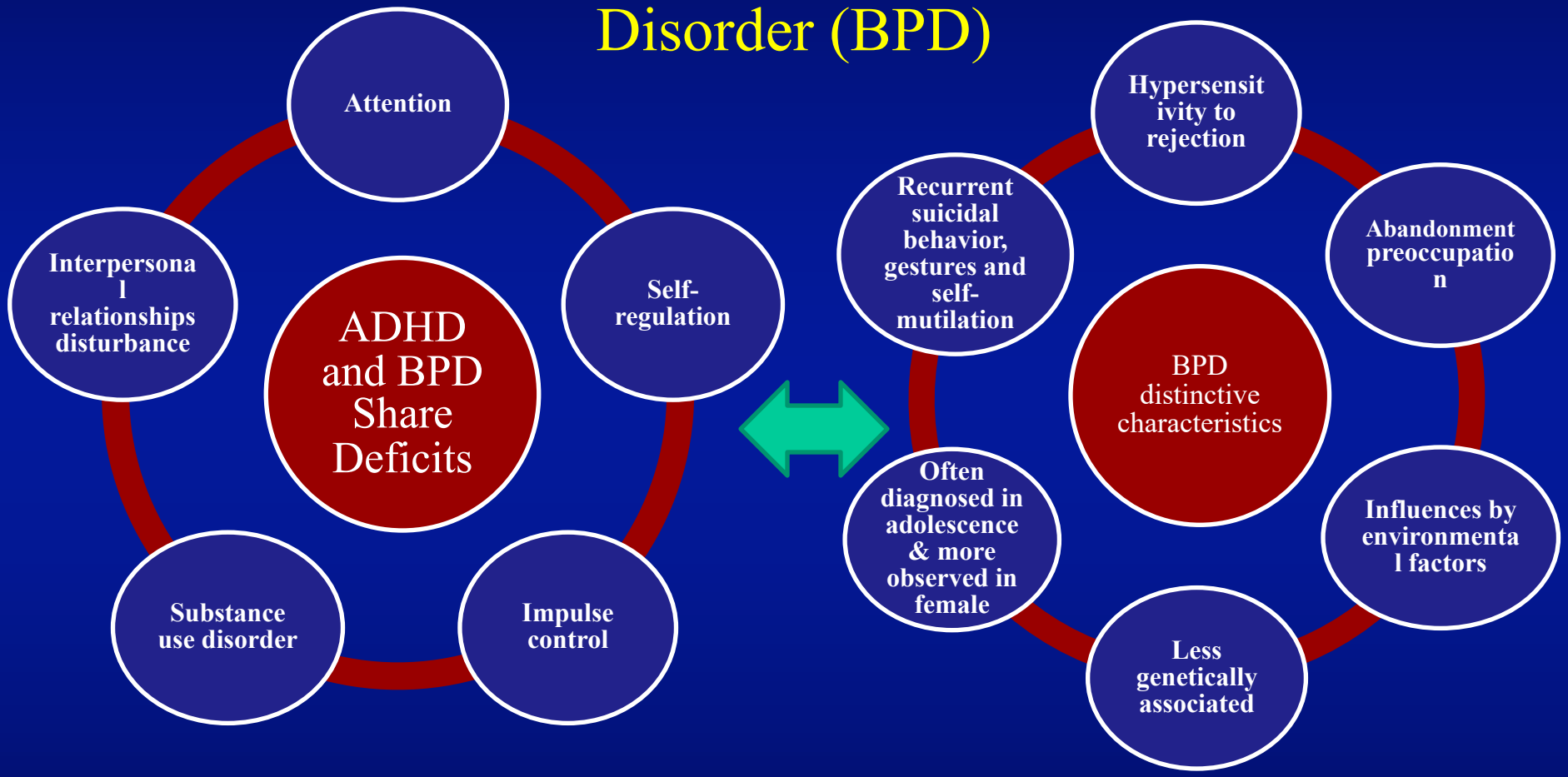
TABLE 3. Irritability in Early Adolescence as Predictor of Disorders at 20-Year Follow-Up, Controlling for Scaled Symptom Scores at Baseline[a]

	Adjustment for Baseline Scaled Score							
	Major Depressive Disorder Score		Overanxious Disorder Score		Oppositional Defiant Disorder Score		Conduct Disorder Score	
Disorder in Adulthood	Odds Ratio	95% CI	Odds Ratio	95% CI	Odds Ratio	95% CI	Odds Ratio	95% CI
Major depressive disorder	1.26	0.98–1.63	1.37*	1.08–1.76	1.3	0.98–1.74	1.31*	1.02–1.67
Generalized anxiety disorder	1.85*	1.22–2.84	2.07**	1.39–3.10	1.92*	1.19–3.10	1.93*	1.27–2.92
Dysthymia	1.92**	1.20–3.06	2.02**	1.33–3.05	2.03*	1.18–3.46	1.80**	1.16–2.82

[a] All logistic regression models report unit-based increases in irritability associated with increases in the odds of disorder in adulthood, adjusted for age, sex, and family socioeconomic status. Imputed N=776.

*p<0.05; **p<0.01.

Features of ADHD and Borderline Personality Disorder (BPD)



A.Fossati,, PS-03, 2011

- Can J Psychiatry. 2015 Feb; 60(2): 42–51.

- **The Pharmacological Management of Oppositional Behaviour, Conduct Problems, and Aggression in Children and Adolescents With Attention-Deficit Hyperactivity Disorder, Oppositional Defiant Disorder, and Conduct Disorder: A Systematic Review and Meta-Analysis. Part 1: Psychostimulants, Alpha-2 Agonists, and Atomoxetine**
- Tamara Pringsheim, MD, MSc,1 Lauren Hirsch, BSc (MSc Candidate),2 David Gardner, PharmD, MSc,3 and Daniel A Gorman, MD4

Figure 1b Psychostimulants, compared with placebo, for aggression, oppositional behaviour, and conduct problems as measured by parents in youth with attention-deficit hyperactivity disorder, with and without oppositional defiant disorder, and conduct disorder

Study or subgroup	Psychostimulants Mean	SD	Total	Placebo Mean	SD	Total	Weight	SMD IV, Random, 95% CI
Findling et al[13]	4.95	3.17	240	6.9	3.18	39	12.4%	-0.61 [-0.96, -0.27]
Gadow et al[19]	1.3	1.5	71	2.1	1.9	71	12.7%	-0.46 [-0.80, -0.13]
Gorman et al[16]	0.43	0.52	19	0.51	0.83	19	6.0%	-0.11 [-0.75, 0.52]
Gorman et al[16]	0.68	0.56	22	1.4	0.84	22	6.1%	-0.99 [-1.62, -0.36]
Greenhill et al[12]	1.04	0.78	165	1.33	0.86	165	16.7%	-0.35 [-0.57, -0.13]
Pelham et al[9]	1.83	1.29	27	4.1	2.89	27	7.0%	-1.00 [-1.57, -0.43]
Sinzig et al[14]	0.8	0.63	43	1.04	0.64	42	9.9%	-0.37 [-0.80, 0.05]
Wilens et al[10]	0.188	0.145	87	0.247	0.206	90	13.9%	-0.33 [-0.63, -0.03]
Wolraich et al[11]	4.95	3.86	192	8.6	4.82	90	15.2%	-0.87 [-1.13, -0.61]
Total (95% CI)			866			565	100.0%	**-0.55 [-0.73, -0.36]**

Heterogeneity: $\tau^2 = 0.04$; $X^2 = 18.03$, $df = 8$ ($P = 0.02$); $I^2 = 56\%$
Test for overall effect, $z = 5.85$ ($P < 0.001$)

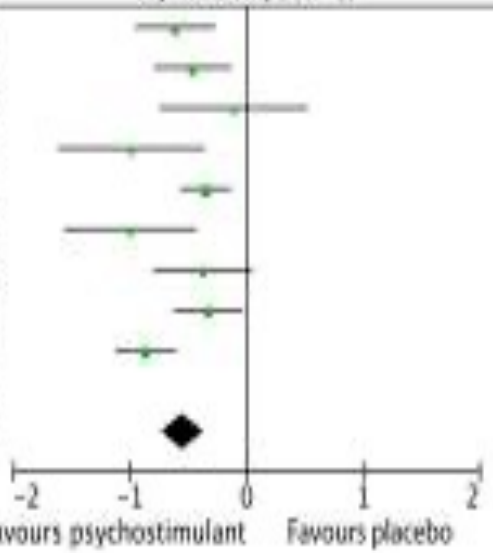


Figure 2 Clonidine, compared with placebo, for oppositional behaviour and conduct problems in youth with attention-deficit hyperactivity disorder, with and without oppositional defiant disorder, and conduct disorder

	Clonidine			Placebo				SMD
Study or subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Agarwal et al[21]	4.1	2.7	9	6.7	5.69	10	6.5%	-0.55 [-1.47, 0.37]
Hazel and Stuart[22]	-5.1	6.6	102	-3.6	6.3	95	70.2%	-0.23 [-0.51, 0.05]
Kollins et al[24]	1.12	0.68	38	1.32	0.56	29	23.3%	-0.31 [-0.80, 0.17]
Total (95% CI)			**149**			**134**	**100.0%**	**-0.27 [-0.51, -0.04]**

Heterogeneity: $X^2 = 0.45$, $df = 2$ ($P = 0.80$); $I^2 = 0\%$
Test for overall effect, $z = 2.26$ ($P = 0.02$)

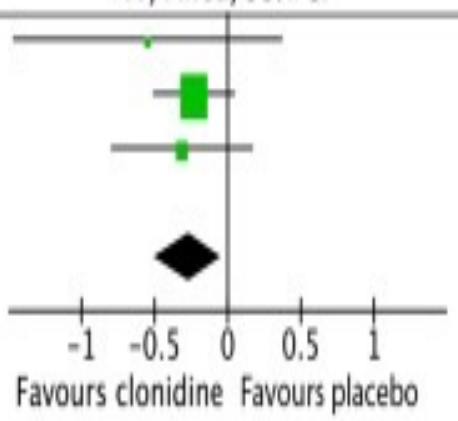
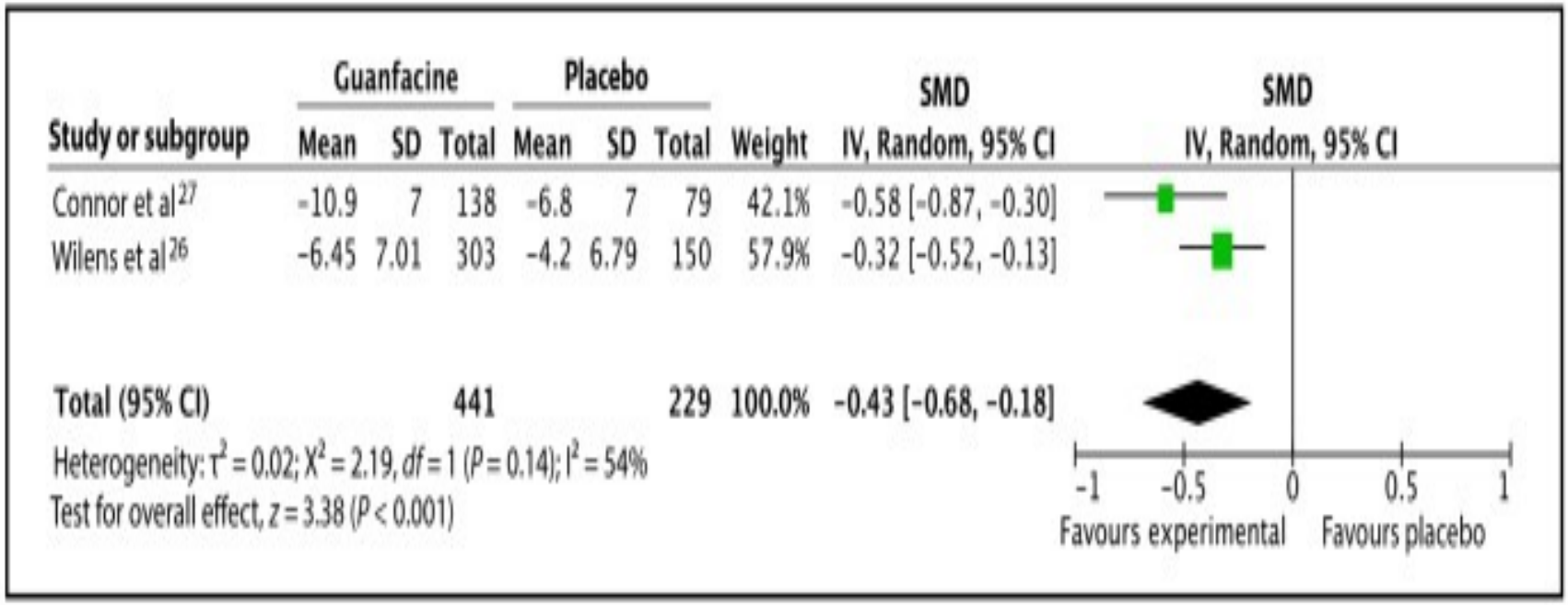
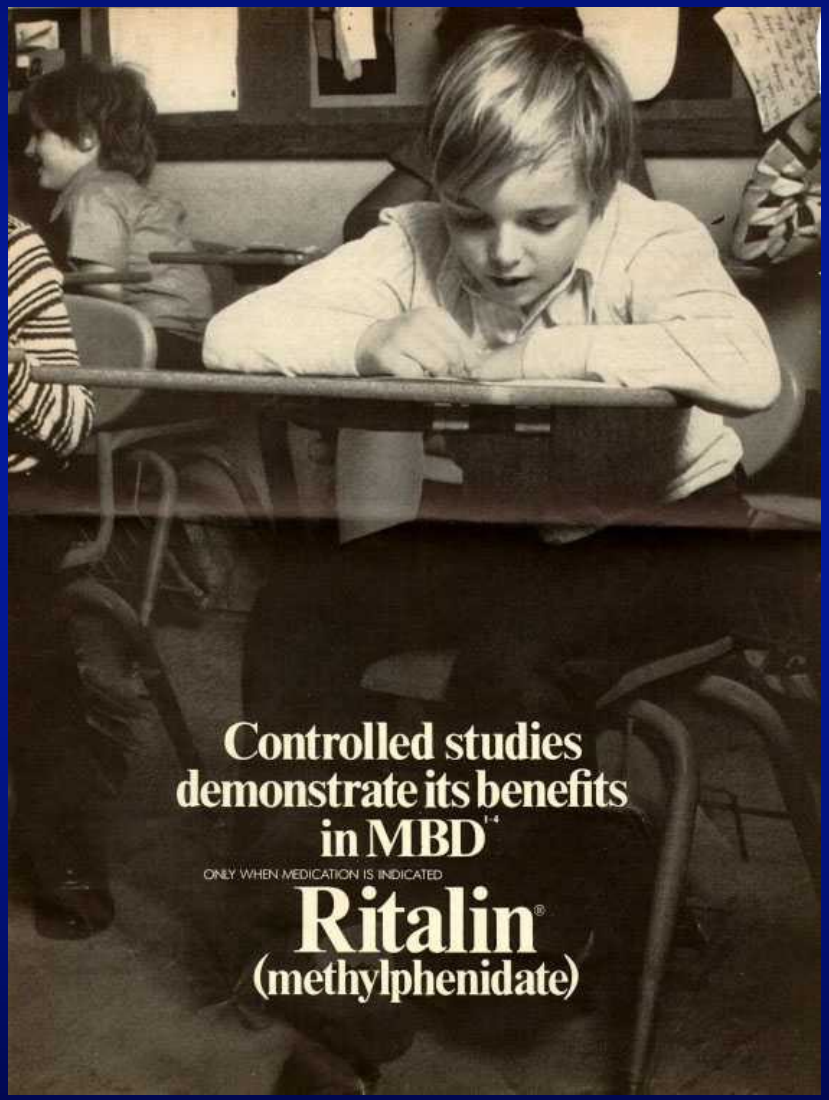


Figure 3 Guanfacine, compared with placebo, for oppositional behaviour in youth with attention-deficit hyperactivity disorder with and without oppositional defiant disorder



This was in 1974: where are we at?



Stimulants and Misuse

Clinical Implications

Among the medications used for the treatment of ADHD, psychostimulants have the most evidence for efficacy in the treatment of oppositional behaviour, conduct problems, and aggression.

There is evidence to support the use of guanfacine and atomoxetine for oppositional behaviour, though effect sizes are small to moderate.

The effect of clonidine on oppositional behaviour and conduct problems may not be clinically significant.

Limitations

There are a very limited number of studies of guanfacine and clonidine for the treatment of oppositional behaviour, conduct problems, and aggression.

- Can J Psychiatry. 2015 Feb; 60(2): 52–61.

- **The Pharmacological Management of Oppositional Behaviour, Conduct Problems, and Aggression in Children and Adolescents With Attention-Deficit Hyperactivity Disorder, Oppositional Defiant Disorder, and Conduct Disorder: A Systematic Review and Meta-Analysis. Part 2: Antipsychotics and Traditional Mood Stabilizers**

- Tamara Pringsheim, MD, MSc, Lauren Hirsch, BSc (MSc Candidate),David Gardner, PharmD, MSc and Daniel A Gorman, MD

Figure 1 Risperidone, compared with placebo, for conduct problems and aggression in youth with subaverage or low IQ and oppositional defiant disorder, conduct disorder, or disruptive behaviour disorder not otherwise specified, with and without attention-deficit hyperactivity disorder

	Risperidone			Placebo				SMD	SMD
Study or subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Aman et al[14]	−15.2	10.6	55	−6.2	11.2	63	43.7%	−0.82 [−1.20, −0.44]	
Buitelaar et al[15]	6.7	6.3	19	8.1	6.9	19	15.3%	−0.21 [−0.85, 0.43]	
Snyder et al[13]	−15.8	11.2	53	−6.8	11.2	57	41.0%	−0.80 [−1.19, −0.41]	
Total (95% CI)			**127**			**139**	**100.0%**	**−0.72 [−0.97, −0.47]**	

Heterogeneity: $X^2 = 2.90$, $df = 2$ ($P = 0.23$); $I^2 = 31\%$
Test for overall effect, $z = 5.64$ ($P < 0.001$)

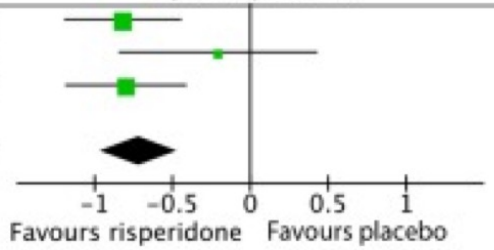


Figure 2 Risperidone, compared with placebo, for disruptive behaviour and aggression in youth with oppositional defiant disorder or conduct disorder, with and without attention-deficit hyperactivity disorder

	Risperidone			Placebo				SMD	SMD
Study or subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Aman et al[14]	10.7	9	84	17.8	15.4	84	90.2%	−0.56 [−0.87, −0.25]	
Findling et al[20]	−1.65	1.26	10	−0.16	1.71	10	9.8%	−0.95 [−1.89, −0.01]	
Total (95% CI)			**94**			**94**	**100.0%**	**−0.60 [−0.89, −0.31]**	

Heterogeneity: $X^2 = 0.60$, $df = 1$ ($P = 0.44$); $I^2 = 0\%$
Test for overall effect, $z = 4.00$ ($P < 0.001$)

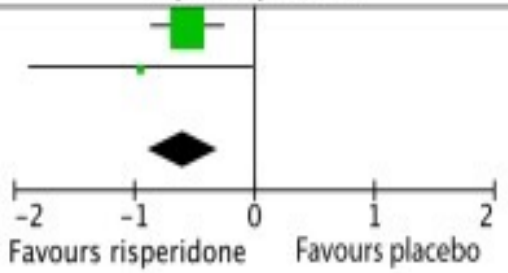


Figure 3 Lithium, compared with placebo, for aggression in youth with conduct disorder

Study or subgroup	Lithium Events	Lithium Total	Placebo Events	Placebo Total	Weight	OR M-H, Fixed, 95% CI
Campbell et al [26]	17	25	10	25	61.0%	3.19 [1.00, 10.17]
Malone et al [25]	16	20	6	20	22.9%	9.33 [2.18, 39.96]
Rifkin et al [24]	3	14	1	12	16.1%	3.00 [0.27, 33.49]
Total (95% CI)		**59**		**57**	**100.0%**	**4.56 [1.97, 10.56]**
Total events	36		17			

Heterogeneity: $X^2 = 1.41$, $df = 2$ ($P = 0.49$); $I^2 = 0\%$

Test for overall effect, $z = 3.55$ ($P < 0.001$)

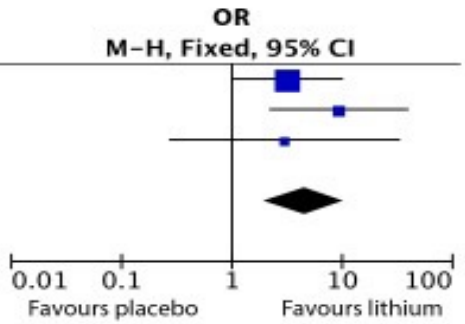
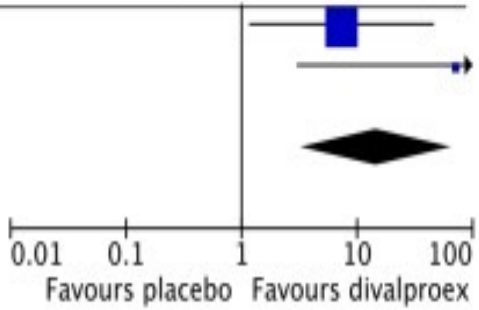


Figure 4 Divalproex, compared with placebo, for aggressive behaviour in youth with oppositional defiant disorder or conduct disorder, with and without attention-deficit hyperactivity disorder

Study or subgroup	Divalproex Events	Divalproex Total	Placebo Events	Placebo Total	Weight	OR M-H, Fixed, 95% CI
Blader et al [27]	8	14	2	13	88.7%	7.33 [1.16, 46.23]
Donovan et al [28]	8	10	0	10	11.3%	71.40 [3.00, 1696.74]
Total (95% CI)		**24**		**23**	**100.0%**	**14.60 [3.25, 65.61]**
Total events	16		2			

Heterogeneity: $X^2 = 1.50$, $df = 1$ ($P = 0.22$); $I^2 = 33\%$

Test for overall effect, $z = 3.50$ ($P < 0.001$)



Clinical Implications

There is evidence to support the clinical efficacy of risperidone for the treatment of aggressive behaviour in youth with ODD and CD, with and without ADHD. Evidence supporting the use of other antipsychotics and mood stabilizers for this purpose is of low quality. Adverse effects related to risperidone use should be strongly considered prior to prescribing it to children.

Limitations

There are a limited number of studies of antipsychotics and mood stabilizers for the treatment of aggression in youth with ADHD, ODD, and CD.

	ISRS	Dose de départ*	Paliers	Dose quotidienne maximum	Présentation	Preuve d'efficacité tirées d'ERC	Générique ?
Première intention	Fluoxétine	10 mg/jour	10-20 mg	60 mg	comprimés de 10 mg, pulvules de 10, 20, 40 mg et pulvules hebdomadaires de 90 mg et sous forme liquide	Oui**	Oui
	Sertraline	25 mg/jour	12,5-25 mg	200 mg	25, 50, 100 mg en comprimés et sous forme liquide	Oui	Oui
Seconde intention	Citalopram	10 mg/jour	10 mg	40 ~~60~~ mg	20, 40 mg en comprimés et sous forme liquide	Oui	Oui
	Escitalopram	5 mg/jour	5 mg	20 mg	5, 10, 20 mg en comprimés et sous forme liquide	Oui	Oui
	Fluvoxamine	25-50 mg/jour, puis b.i.d.	25-50 mg	300 mg	25, 50, 100 mg en comprimés et sous forme liquide	Non	Oui

Tous les ISRS énumérés sont contre-indiqués avec les IMAO; la fluvoxamine est aussi contre-indiquée avec la terfénadine, l'astémizole et le pimozide.

* Envisager de débuter le traitement à dose plus faible chez les jeunes enfants; ** La fluoxétine est approuvée par la FDA.
† Trois essais considérés négatifs par la FDA et la MHRA (*Medicines and Healthcare products Regulatory Agency* du R.-U.)