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Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

TREATING ADHD IN THE SETTING OF BIPOLAR DISORDER

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project ECHO

SPEAKER DISCLOSURES

No conflicts of interest

PLANNER DISCLOSURES

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ACKNOWLEDGE THE LAND OF THE COAST SALISH PEOPLES, WHICH TOUCHES THE SHARED WATERS OF ALL TRIBES AND BANDS WITHIN THE DUWAMISH, SUQUAMISH, TULALIP AND MUCKLESHOOT NATIONS.

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OBJECTIVES

1. Prevalence of Comorbid ADHD and Bipolar
2. Diagnostic Clarification
3. Treatment Options

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INDEPENDENT PREVALENCE

- Bipolar Disorder Spectrum [1]
  - 1-3% of U.S adults with bipolar disorder
  - Equal ratio of males: females

- ADHD [2]
  - Childhood prevalence of 4–7%
  - Prevalence in adulthood is around 2.5%
  - Systematic review suggest childhood ADHD persists into adulthood in 15–60% of cases
  - Child and adolescents 3:1 male: female
  - Adult decrease to 2:1 male: female

COMORBID ADHD AND BIPOLAR [3,4]

- Prevalence of comorbid ADHD and Bipolar
  - 1 in 6 people with Bipolar have comorbid ADHD (17.11 %; 95 % CI: 13.05–21.59).
  - 1 in 13 people with ADHD has comorbid bipolar disorder (7.95 %; 95 % CI: 5.31–11.06)

- Implications:
  - Age of Bipolar Disorder onset occurred ~4 years earlier in patients with comorbid ADHD (3.96 years; 95 % CI: 2.65–5.26, $p < 0.001$).
  - Higher comorbid anxiety disorders, functional and social impairments
  - Underdiagnosis and undertreatment
  - Higher risk of substance use

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RESEARCH LIMITATIONS

- Diagnostic systems (DSM-5, ICD)
- Geographical Difference
- Cultural and ethnic factors
- Methodological factors
- Sample size

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DIAGNOSIS

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OVERLAPPING DIAGNOSTIC FEATURES

- Talkative
- "Racing thoughts"
- Impulsivity
- Hyperactivity
- Attention, concentration, "focus" problems
- Risk-taking behavior
- Functional Impairment
- Higher rate of substance use, eating disorders
- Sleep irregularities
- Irritability, restlessness
- Sensory sensitivities

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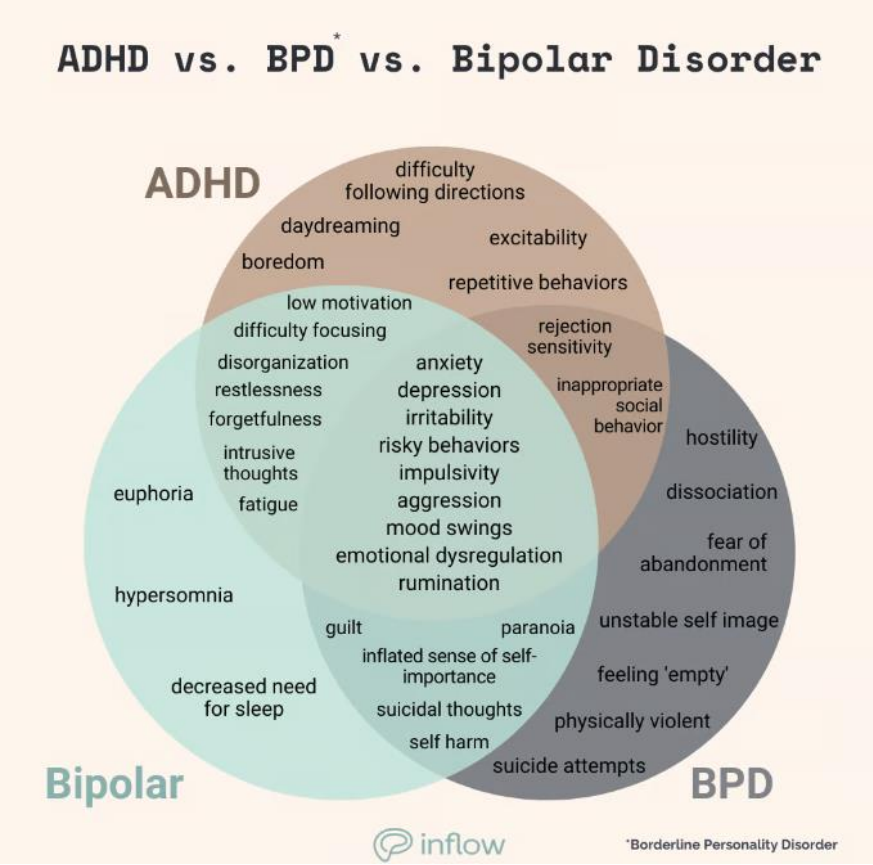
WHAT ELSE DOES THAT LOOK LIKE?

- Trauma
- Substance use disorders
- Personality Disorders
- Anxiety
- Depression



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RISK FACTORS

- Genetic overlap, epigenetic
- Neuronal signaling
- Perinatal risk factors
- Childhood maltreatment

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DISTINGUISHING FEATURES

Table 1

Similarities and differences between ADHD and BD.

Characteristic	ADHD	BD
Age at onset	Childhood	Early adulthood
Course	Stable	Episodic
Symptoms	• Labile, dysphoric mood • Reduced self-esteem • Distractibility perceived as thought wandering, without objective acceleration • Restlessness, fidgetiness	• Persistently euphoric, elevated or irritable mood • Inflated self-esteem or grandiosity • Distractibility due to acceleration of thought • Increased goal-directed activity
Sleep	Usually not affected	Decreased need to sleep
Sexuality	Not affected	Increased (hypo- or mania)
Psychosis	Absent	Possible

Salvi V, et al, 2021 May

DIAGNOSTIC CASE

- 23 year old male with previous diagnosis of bipolar 2 and ADHD on Lamotrigine 50mg and Adderall 5mg BID, feeling depressed
- Next steps?

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WHO KNOWS?

What can you do?

- Screening Tools
- Get more information: collateral information, family history
- Observe over time, mood tracker
- Sleep hygiene
- Reduce risk factors for safety
- Reduce substances during observation period.
- Address stressors
- Engage in therapy
- Start a medication?

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TREATMENT OPTIONS

- Bipolar:
  - Mood stabilizers
  - Antipsychotics

- ADHD
  - Stimulants*
  - Non-stimulants:
    - SSRI/SNRIs (venlafaxine, atomoxetine , viloxazine, des
    - Bupropion
    - Alpha-agonist*

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POLL:

- Who would recommend stimulant treatment in bipolar disorder?

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WHAT'S THE RISK?

Early studies showed concern for stimulant induced mania in animal studies

Population-Based study in Canada (Cressman, 2015):

- Stimulant initiation was associated with increased risk of hospitalization for psychosis or mania

Large-scale, register-based study from Sweden (Viktorin A, 2017):

- Methylphenidate treatment alone has increased risk for treatment emergent mania
- Risk lower when co-administrated with mood stabilizers
- Follow up study showed no increased risk (Jefsen, Oskar Hougaard MD, 2022)

Only 3 small placebo-controlled trials

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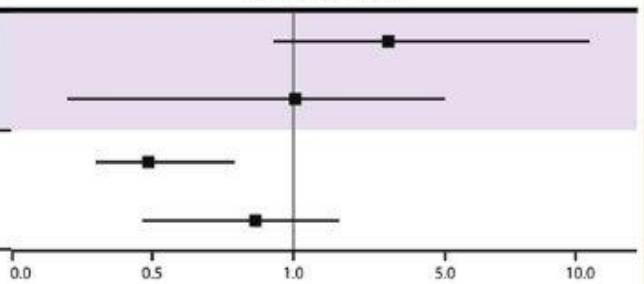
RISK OF TREATMENT-EMERGENT MANIA (VIKTORIN A, 2017)

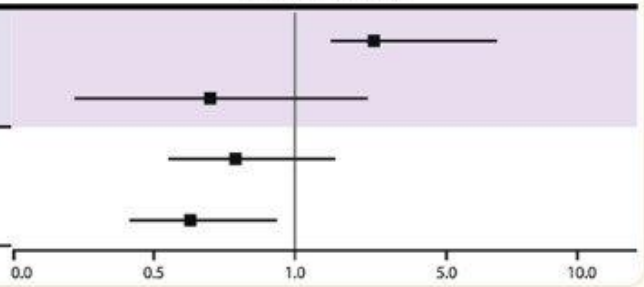
Current Study: Methylphenidate*

Years	Sample Size	Group	Group Number	Group Percent	Mania rate	Period	Hazard Ratio	P-value	95% CI	Forest Plot
2006 - 2014	2,307	No stabilizer	718	31.1	24 (0.03)	0-3 months	3.33	0.067	0.92 - 12.11	
						3-6 months	1.00	1.000	0.20 - 4.95	
		Stabilizer	1,103	47.8	144 (0.13)	0-3 months	0.48	0.002	0.30 - 0.77	
						3-6 months	0.86	0.640	0.47 - 1.60	



Previous Study: Antidepressants**

Years	Sample Size	Group	Group Number	Group Percent	Mania rate	Period	Hazard Ratio	P-value	95% CI	Forest Plot
2006 - 2009	3,240	No stabilizer	1,117	34.5	42 (0.04)	0-3 months	2.83	0.028	1.12 - 7.19	
						3-9 months	0.71	0.567	0.23 - 2.26	
		Stabilizer	1,641	50.6	281 (0.17)	0-3 months	0.79	0.214	0.54 - 1.15	
						3-9 months	0.63	0.020	0.42 - 0.93	



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MAIN TAKE AWAY

- Mood Stabilize and then consider ADHD treatment
  - If stimulant, methylphenidate
  - Monitor symptoms closely
  - Educate about mania risk

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OTHER TREATMENT OPTIONS FOR ADHD

- Alpha-2 agonist
  - Clonidine
  - Guanfacine
- Modafinils*
- Omega-3s

Treatments for ADHD in Bipolar Disorder

Medication	Dosage	Notes
Clonidine and guanfacine	ER: 0.1–0.4 mg/day.[1] IR: 0.1–0.3 mg/day. Transdermal (clonidine only): 0.1–0.3 mg/day weekly patch.	Start with ER, which is FDA approved for ADHD and generic. Start QHS and divide BID at higher doses. The weekly clonidine patch improves on tolerability. Taper off gradually to avoid rebound hypertension.
Modafinils	Modafinil: 100–200 mg/day. Armodafinil: 150–250 mg/day.	Armodafinil has a longer duration and steadier effects than modafinil. Find low-cost options at goodrx.com if not covered by insurance.
Omega-3s	EPA + DHA = 1000–3000 mg/day, with EPA ≥ 2 times DHA amount.	Reliable brands include Viva Naturals (Amazon), Member's Mark (Sam's Club), and Kirkland (Costco) (15–25 cents/day).
Stimulants	Prefer methylphenidate over amphetamines. Start with methylphenidate ER 18 mg/day.	Use lowest effective dose. If tolerance develops, revisit the diagnosis before raising it further.
Lifestyle	Aerobic exercise, Mediterranean diet, good sleep, and mindfulness improve both ADHD and mood disorders.	

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MANIA?

- Anti-Mania Medications:
  - Lithium
  - Valproate
  - Antipsychotics
- Agitation
  - Benzodiazepines

Drug	Acute mania	Mixed mania	Prevention of mania after mania	Prevention of depression after mania
Lithium	+++	+	+++	++
Valproate	+++	++	+	+
Carbamazepine	+++	++	+	+
Lamotrigine	-	-	+	+++
Gabapentin	-	-	?	?
Topiramate	-	?	?	?
Oxcarbazepine	+	+	+	?
Licarbazepine	-	-	?	?
Chlorpromazine	++	+	?	?
Haloperidol	+++	++	?	?
Clozapine	+	+	?	?
Risperidone	+++	+	+	?
Olanzapine	+++	++	+++	++
Quetiapine	+++	+	+++	+++
Ziprasidone	+++	++	?	?
Aripiprazole	+++	++	+++	?

SUMMARY

1. Comorbidity of ADHD and Bipolar ~20%
2. Clarify the diagnosis
3. Stabilize mood, then treat ADHD

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THANK YOU!

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RESOURCES

1. https://www.nimh.nih.gov/health/statistics/attention-deficit-hyperactivity-disorder-adhd
2. https://www.nimh.nih.gov/health/statistics/attention-deficit-hyperactivity-disorder-adhd
3. Salvi V, Ribuoli E, Servasi M, Orsolini L, Volpe U. ADHD and Bipolar Disorder in Adulthood: Clinical and Treatment Implications. Medicina (Kaunas). 2021 May 10;57(5):466. doi: 10.3390/medicina57050466. PMID: 34068605; PMCID: PMC8151516.
4. Schiweck C, Arteaga-Henriquez G, Aichholzer M, Edwin Thanarajah S, Vargas-Cáceres S, Matura S, Grimm O, Haavik J, Kittel-Schneider S, Ramos-Quiroga JA, Faraone SV, Reif A. Comorbidity of ADHD and adult bipolar disorder: A systematic review and meta-analysis. Neurosci Biobehav Rev. 2021 May;124:100-123. doi: 10.1016/j.neubiorev.2021.01.017. Epub 2021 Jan 27. PMID: 33515607.
5. Cressman, Alex M. MSc*†; Macdonald, Erin M. MSc*; Huang, Anjie MSc*; Gomes, Tara MHSc*‡§‖‖; Paterson, Michael J. MSc*§; Kurdyak, Paul A. MD, PhD*†¶; Mamdani, Muhammad M. MPH, PharmD*‡§‖‖#; Juurlink, David N. MD, PhD*†‡§** for the Canadian Drug Safety and Effectiveness Research Network. Prescription Stimulant Use and Hospitalization for Psychosis or Mania: A Population-Based Study. Journal of Clinical Psychopharmacology 35(6):p 667-671, December 2015. | DOI: 10.1097/JCP.0000000000000406
6. Viktorin A, Rydén E, Thase ME, Chang Z, Lundholm C, D'Onofrio BM, Almqvist C, Magnusson PK, Lichtenstein P, Larsson H, Landén M. The Risk of Treatment-Emergent Mania With Methylphenidate in Bipolar Disorder. Am J Psychiatry. 2017 Apr 1;174(4):341-348. doi: 10.1176/appi.ajp.2016.16040467. Epub 2016 Oct 3. Erratum in: Am J Psychiatry. 2016 Nov 1;173(11):1154. PMID: 27690517; PMCID: PMC6641557.
7. Jefsen, Oskar Hougaard MD[1,2,3]; Østergaard, Søren Dinesen PhD[1,2]; Rohde, Christopher MD[1,2]. Risk of Mania After Methylphenidate in Patients With Bipolar Disorder. Journal of Clinical Psychopharmacology 43(1):p 28-34, 1/2 2023. | DOI: 10.1097/JCP.0000000000001631
8. Galanter CA, Carlson GA, Jensen PS, Greenhill LL, Davies M, Li W, Chuang SZ, Elliott GR, Arnold LE, March JS, Hechtman L, Pelham WE, Swanson JM. Response to methylphenidate in children with attention deficit hyperactivity disorder and manic symptoms in the multimodal treatment study of children with attention deficit hyperactivity disorder titration trial. J Child Adolesc Psychopharmacol. 2003 Summer;13(2):123-36. doi: 10.1089/104454603322163844. PMID: 12880507.
9. Vieta E, Sanchez-Moreno J. Acute and long-term treatment of mania. Dialogues Clin Neurosci. 2008;10(2):165-79. doi: 10.31887/DCNS.2008.10.2/evieta. PMID: 18689287; PMCID: PMC3181868.

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