Underpinnings of Adult ADHD:

Prevalence, Comorbidities, Diagnosis and Treatment

Sara K Binder, MD FRCPC

Disclosures: Sara K. Binder, MD, FRCPC

- Janssen – Speaker honoraria, Ad Board
- Shire – Speaker honoraria, Ad Board, Intl Sponsorship
- Purdue – Unrestricted Educational Grant, Intl Sponsorship

Objectives

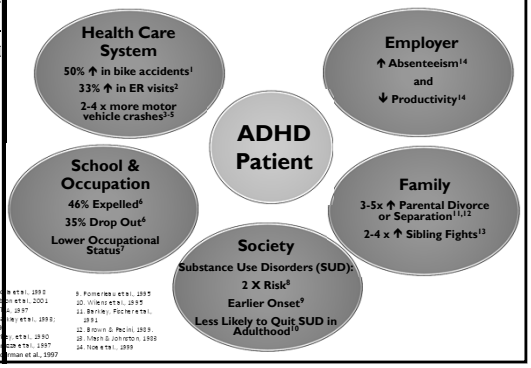
Adult ADHD:

- Prevalence
- Impact
- Symptom Identification
- Diagnostic clinical tools
- Common comorbidities – DDx
- First-line treatments

How might ADHD impact my practice

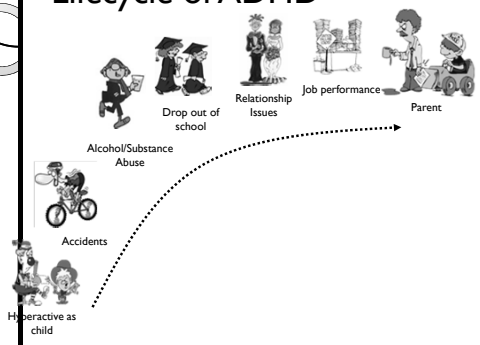
?

Impact of Untreated and Under-Treated ADHD



1. DiScala et al., 1998
2. Lieshout et al., 2001
3. NHTSA, 1997
4-5. Barkley et al., 1993; 1996
6. Barkley, et al., 1990
7. Murphy et al., 1997
8. Biederman et al., 1997
9. Pomerleau et al., 1995
10. Wilens et al., 1995
11. Barkley, Fischer et al., 1991
12. Brown & Pacini, 1989.
13. Mash & Johnston, 1983
14. Noe et al., 1999

Lifecycle of ADHD



7

ADHD Sufferers in Canada in 2011

(Statistics Canada)

	ADHD in children, teens (age 5–19)	ADHD in adults (age 20–64)
Total Population *(estimates)*	5,931,717	21,550,449
Prevalence [%]	6%	4.4%
Patients with ADHD	355,903	948,219
% Diagnosed & Treated	33%	7%
Patients Diagnosed & Treated	117,448	66,375

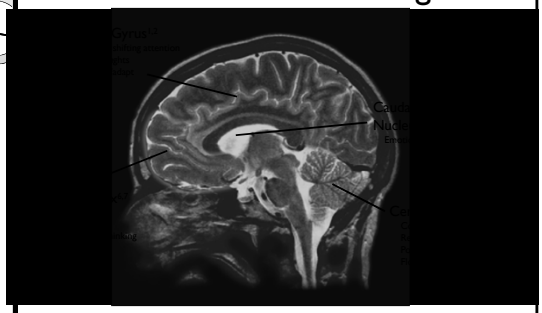
How many adults are left untreated? 881,844

Kessler RC et al. Am J Psychiatry 2006; Statistics Canada, 2004 projected to 2005; % diagnosed calculated based on estimate of treated patients in Canada

8

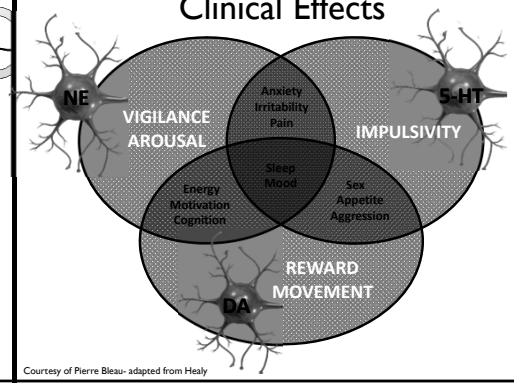
Understanding the Neurobiology of ADHD

Regions of the Brain Involved in Executive Functioning



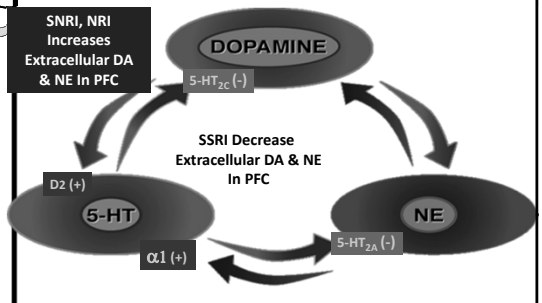
1. MacDonald et al. Science 2000;288:1835-8. 2. Kennerley et al. Nature Neuroscience 2006;9:940-7.
3. Gao et al. Science 1996;272:545-7. 4. Rapoport et al. J Neuropsychiatry Clin Neurosci 2000;12:193-8.
5. Tremols et al. Psychiatry Res 2008;163:270-8. 6. Rubia et al, Am J Psychiatry 2009;166:83-94.
7. Wolf et al. Hum Brain Mapp 2008.

Monoamines Related to Clinical Effects



Courtesy of Pierre Bleau- adapted from Healy

Monoamines Communicate



Trivedi MH, Hollander E, Nutt D, Blier P. Clinical evidence and potential neurobiological underpinnings of unresolved symptoms of depression. J Clin Psychiatry 69:, February 2008

IDENTIFICATION

13

Symptom Buckets

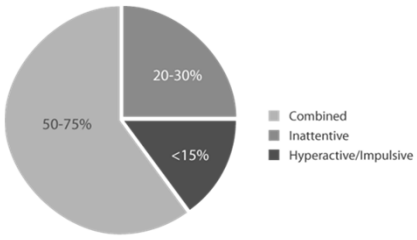
COMBINATION of symptoms = MAJORITY of patients (50-75%)

Inattentive type increases with age while hyperactive type decreases

Association AP. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition: DSM-IV-TR®. American Psychiatric Pub; 2000.

14

Prevalence of ADHD Presentations



American Psychiatric Association (APA) (1994), Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV). Washington, D.C.: American Psychiatric Publishing, Inc.

ADHD - Inattention Symptoms

Childhood

- Difficulty sustaining attention for homework, chores
- Loses things
- Appears to be not listening
- Trouble with follow through
- Easily distracted
- Daydreams

Adulthood

- Difficulty sustaining attention in meetings, at work and for household responsibilities
- Disorganized, poor time management
- Inefficient, slow to complete work
- Procrastinate
- Trouble with follow through – don't do what they promised
- Complain of poor memory, forgetful

1. Adler LA. J Clin Psychiatry. 2004. 2. Association AP. 2. DSM-IV-TR®. American Psychiatric Pub; 2000.

16

ADHD - Hyperactive Symptoms

Childhood

- Can't stay in seat, squirming, fidgeting, always on the go
- Can't work or play quietly, runs, climbs excessively
- Intrudes and interrupts others
- Talks excessively
- Restless
- Impatient

Adulthood

- Can't sit through meetings (checking email, scribbling notes)
- Toe tapping, leg bouncing, chew nails, click pens
- Drives fast, likes active jobs
- Always on the go
- Inner restlessness

1. Adler LA. J Clin Psychiatry. 2004. 2. Association AP. 2. DSM-IV-TR®. American Psychiatric Pub; 2000..

17

ADHD – Impulsive Symptoms

Childhood

- Can't wait turn, blurts out answers
- Intrudes and interrupts others
- Quits school, gets into trouble with law
- Rushes into things
- Takes risks
- Accident prone
- Impatient/interrupts

Adulthood

- Doesn't think about consequences
- Makes inappropriate comments ("no mental filter")
- Blurts/Interrupts
- Risk taking – speeding, spending, substances, sex
- Relationship and marital difficulties
- Frequent job/career changes
- Impatient (hates waiting in lines)

1. Adler LA. J Clin Psychiatry. 2004. 2. Association AP. 2. DSM-IV-TR®. American Psychiatric Pub; 2000..

18

Case 1: Marie

- 36y/o, married mother of 2 boys – 7y & 4y
- 6 months pregnant
- Works full time in healthcare, masters level education
- Binge Eating D/O from early childhood
- First Depressive episode in late teens
- Manic Episode with psychotic features at 20y/o in the context of moving away from home to work in high stress job, sleep deprivation, few supports
- Hospitalized, diagnosed with Bipolar I and treated with Lithium

Past Psychiatric History

- For the next few years intermittently compliant with Li
- Manic-like symptoms in the fall and depressive symptoms in the winter, no further hospitalizations
- Initiated individual therapy and Eating D/O treatment
- D/C Lithium after first child, stable for last 7 years

Current Symptoms

- Struggles at work due to disorganization, procrastination, behind on paperwork
- Difficulty maintaining household chores, kids schedules, groceries, bills etc
- Binge eating to cope with intense emotions
- Relationship struggles with spouse related to parenting and household management
- Mild depressive Sxs related to situation
- No current manic symptoms

Current Symptoms

- Anxiety screen:
  - Constant worries about feeling inadequate, not fitting in, work performance, not keeping up
  - Future worries about children, one of whom has ASD and ADHD
  - Long history of fearing judgment and criticism, avoidance of crowds and social gatherings
  - No OCD, PTSD or Panic D/O
- Substance Use:
  - Minimal Etoh pre-pregnancy, no drugs
  - 4 cups of coffee/day pre-pregnancy, currently 2 cups/day

ADHD Screening

- Childhood:
  - Lifelong problems with organization and time management
  - Never able to read a full book, only abstracts
  - Trouble attending to details, "Big Ideas Person"
  - Always in trouble with parents due to disorganization
  - Never performed as well academically as her IQ would suggest
  - "faked her way through school"
  - Put in huge efforts with limited results
  - Always procrastinated
  - Shy and a "daydreamer" at school

ADHD Screening

- Adulthood:

-Failed some courses in university, academic probation

-Not reaching her potential at work

-Behind on paperwork

-Easily overwhelmed by household tasks/chores

-Has needed to over-control her environment to cope

-Always loses keys, phone, wallet, glasses

-Often late or forgets appointments

Marie

- Medical History:
  - No serious head injury or LOC, no seizure history
  - Hypothyroid while on Li and briefly treated with Synthroid
  - Normal BP, no cardiac history
- Family Psychiatric History
  - Father ADHD, ASD, OCD
  - Mother significant mood dysregulation, ? BPD
  - Sister – severe anxiety
  - Son ASD, ADHD

Differential Diagnosis

- ADHD, Inattentive presentation
- Social Anxiety D/O
- Binge Eating D/O
- R/O Generalized Anxiety D/O
- Historial Dx of Bipolar I

What next?...

- ADHD screening
  - ASRS
  - Barkley Childhood and Current Self/Other Symptom Scales
  - Weiss Functional Impairment Rating Scale
- Collateral from Spouse/Parents
  - Mood log to R/O Bipolar D/O

SCREENING

28

When to Screen?

Patients presenting with:

- Major Mood and Anxiety D/O (including poor response to treatment)
- Drug abuse or drug dependence
- Family history or children with ADHD
- Poor school performance as a child and/or university (not reaching potential)
- Frequent job changes or moving often
- Frequent driving infractions
- Higher number of accidents than average population
- Forgetfulness (late or missed appointments, trouble with adherence to medications)
- Lack of follow-through on therapeutic "homework"

29

Screening Tools

- ADHD Self-Report Scale (ASRS v1.1)
- Barkley Childhood and Current Symptom Scales
- Wender Utah Rating Scale
- Delta Education Screener
- Jerome Driving Scale
- Weiss Functional Impairment Scale

30

WHAT IS THE NEXT STEP?

31

Questions for Suspected ADHD

Have you ever been diagnosed with ADHD?

- Do you have a family history of ADHD (siblings, children, parents or extended family)?
- Did you have any difficulty in school?
  - Did you daydream or have difficulty paying attention?
  - Did you get your homework done on time?
  - Were you disruptive?

Anything positive – move to Step 2

Do you currently have substantial difficulties with forgetfulness, attention, impulsivity or restlessness that are interfering with your relationships or your success at work?

Anything positive – move to Step 3

Complete ASRS & Complete Diagnostic Interview

McIntosh D, Kutcher S, Binder C, et al. Neuropsychiatr Dis Treat. 2009.

32

ASRS

The ASRS Screener v1.1

1. Inattention	Never	Rarely	Some-times	Often	Very Often
How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?					
How often do you have difficulty getting things in order when you have to do a task that requires organization?					
When you have a task that requires a lot of thought, how often do you avoid or delay getting started?					
How often do you have problems remembering appointments or obligations?					
2. Hyperactivity – Impulsivity					
How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?					
How often do you feel overly active and compelled to do things, like you were driven by a motor?					

Significant items in Red (*p=0.5); Likely to have ADHD with ≥ 4 significant items

World Health Organization

http://www.med.nyu.edu/psych/assets/adhdscreen18.pdf

Adult ADHA Self-Rating Scale (ASRS)

Patient Name: Today's Date:

Please answer the questions below, rating yourself on each of the criteria shown using the scale on the right side of the page. As you answer each question, place an X in the box that best describes how you have felt and conducted yourself over the past 6 months. Please give this completed checklist to your healthcare professional to discuss during today's appointment.

	Never	Rarely	Sometimes	Often	Very Often	
Can't Follow Instructions						Inattentive: D
Poor Organizational Skills						Inattentive: E
Forgetful in Daily Tasks						Inattentive: I
Avoids Tasks Requiring ++ Thinking						Inattentive: F
Fidgets						Hyper/Impulsive: A
Inner Feeling of Driven by a Motor						Hyper/Impulsive: E
Part A						
Careless Mistakes						Inattentive: A
Difficulty Sustaining Attention						Inattentive: B
Poor Listening Skills						Inattentive: C
Loses Things Constantly						Inattentive: G
Easily Distracted						Inattentive: H
Difficulty remaining Seated						Hyper/Impulsive: B
Extreme Restlessness						Hyper/Impulsive: C
Difficulty Relaxing						Hyper/Impulsive: D
Talks Excessively						Hyper/Impulsive: F
Blurts Out before Thinking						Hyper/Impulsive: G
Difficulty Waiting in Turn						Hyper/Impulsive: H
Interrupts Others even if Busy						Hyper/Impulsive: I
Part B						

DSM-5 Diagnostic Criteria

Adapted from ASRS by Tom Janzen, M.D., 2014

5/9 AGE 17+

6/9 AGE <17

5/9 AGE 17+

6/9 AGE <17

HOW TO CONFIRM DIAGNOSIS

36

Attention Deficit Hyperactivity Disorder – DSM 5

- Diagnostic criteria
  (American Psychiatric Association Diagnostic and Statistical Manual (DSM-5)
  - > 5 of 9 symptoms of inattention X > 6 mos.
    and/or
  - > 5 of 9 symptoms of hyperactivity-impulsivity X > 6 mos.
- Onset prior to age 12 years
- Impairment in more than one setting (e.g., both school and home)
- Social, academic, or occupational impairment
- Symptoms not accounted for by another mental disorder such as a psychotic disorder, mood disorder, anxiety disorder, etc.
- Presentations:
  - Inattentive
  - Hyperactive-Impulsive
  - Combined (most common)

DSM—5, American Psychiatric Pub; 2000; Drug Safety and Risk Management Advisory Committee, 2013

37

WHAT ARE COMMON COMORBIDITIES?

38

CANMAT Guidelines 2012 and Comorbidities

- Mood disorders and ADHD frequently co-exist in same families with both disorders, the tendency for comorbidity also is inherited
- Clinicians should routinely assess patients with Bipolar Disorder and MDD for comorbid ADHD and distinguish ADHD from syndromal and subsyndromal mood symptoms

Bond DJ, et al. Ann Clin Psychiatry. 2012.

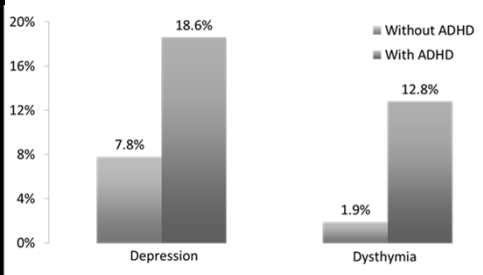
Depression	ADHD
• Episodic • Anhedonia • Consistent low mood (2 weeks) • Poor Concentration • Weight loss/gain • Worthlessness • Low energy • Psychosis (rarely) • Suicidality • Insomnia – initial, mid, term. **Usually occurs in late 20's**	• Childhood onset • Affective Instability (with rapid recovering) • Selective Enthusiasm • Demoralized during life transitions • Talkativeness • Concentration (chronically poor unless really interested) • Initial Insomnia(73%), restless sleep(80%) or sleep/wake reversal **Onset during childhood**

Presentation of Depression and ADHD

Poor concentration, attention and memory, sleep problems, difficulty with task completion

40

Prevalence of Depression in Adults With and Without ADHD



Kessler RC et al. Am J Psychiatry 2006;163(4):716-23.

p<0.05 for both comparisons

ADHD	Bipolar Mood Disorder
• Lifelong • Childhood onset • Reactive mood • Congruent mood • Impulsive changes • 1-2 days of increased goal directed behaviour with decreased sleep related to a deadline/interest/project • Scattered thoughts • Low self-esteem • Family history of ADHD	• Cyclic • Early + late onset • Objective change from baseline • Decreased need for sleep • Increased energy • Non-congruent mood • Grandiosity • Family history of bipolar affective disorder

Presentation of ADHD and Bipolar Mood Disorder

1. Dodson WW. ADDvance Magazine. 2000.
2. State RC. American Journal of Psychiatry. 2002.

42

ADHD	Anxiety
• Childhood onset • Restless • Irritable • Perseveration • Easily overwhelmed • Worries related to untreated ADHD symptoms – losing, forgetting, procrastinating, blurting, interrupting, risk taking	• Excessive worry causing physical symptoms • Panic attacks with fear of recurrence • Fear of being judged • Repetitive, intrusive thoughts • Compulsive behaviours to relieve anxiety • History of trauma with flashbacks, hyperarousal and avoidance

Presentation of ADHD and Anxiety:

Fidgetiness, difficulty concentrating

Anxiety disorder may attenuate impulsivity related to ADHD

3

ADHD	Personality Disorders
• Oblivious • Unable to manage activities of daily living • Self-esteem poor rather than unstable • Non-malicious (remorseful immediately following impulsive act) • Intense affect with quick recovery and no self harm	• Manipulative • Empty • Absence of remorse • Deliberate cruelty • Generates antipathy in others rather than frustration • Lack of empathy • Feelings of emptiness • Fear of abandonment • Self harm • Mood Dysregulation

Differential Diagnosis of Personality Disorders and ADHD

Weiss, Adolescent ADHD, Brown, T.E., 2009. 44

TREATMENT

45

Biological Management

- Establish treatment goals
- Discuss reasonable expectations of treatment, including possible medication side-effects
- Use long-acting stimulants
  - Start with lowest dose
  - Evaluate symptoms/side effects every 2 weeks using ASRS
- Re-evaluate treatment goals

46

CADDRA Guidelines 2014

st Line Recommendations (Adult)

Brand Name	Dosages (mg)	Starting Dose (q.d. a.m.)	Weekly Titration (mg)	Maximum Dose (mg)	Duration of Efficacy (hours)
Adderall XR (mixed amphetamine salts)	5, 10, 15, 20, 25, 30	10	10	20-30 mg	10 - 12
Biphentin (MPH HCL)	10, 15, 20, 30, 40, 50, 60, 80	10-20	10	80	10 - 12
Concerta (OROS MPH)	18, 27, 36, 54	18	18	72	10 - 12
Vyvanse (Lisdexamfetamine)	20, 30, 40, 50, 60	20-30	Clinical Discretion	60	13 - 14

Some patients may respond preferentially to one versus the other class of medications, so if response or side effects to one class of medication are not optimal… switch to the other class of stimulant".

Second-line/adjunctive agent recommendations include the long-acting non-stimulant atomoxetine and short-acting stimulants.

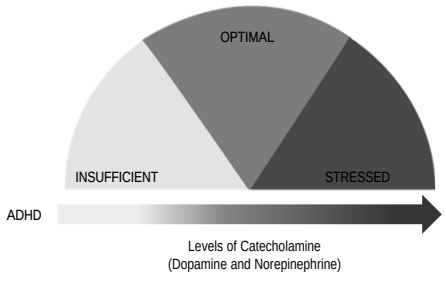
CADDRA: Canadian ADHD Practice Guidelines. www.caddra.ca, 2014

Effect Sizes in Psychiatry

	Effect Size
Atypical Neuroleptics (schiz.)	0.25
SSRI's for Major Depression	0.50
ADHD Medication Nonstimulants (as a group) Extended Release Stimulants*	 0.62 0.95

araone SV. Using a meta-analysis to draw conclusions about ADHD medication effects. merican Psychiatric Association; May 21, 2003; San Francisco, Calif.

Prefrontal Cortex Requires Proper "Tuning" of Catecholamine Levels for Optimal Function



1. Hosenbocus S, Chahal R. J Can Acad Child Adolesc Psychiatry. 2009; 2. Ramos-Quiroga JA, Bosch R, Castells X, et al.. CNS Drugs. 2008; 3. Stahl SM, Stahl SM. Stahl's Essential Psychopharmacology: Neuroscientific Basis and Practical Applications. 2008.

49

Minimize Side Effects

- Establish treatment goals
- Discuss reasonable expectations of treatment, including possible side-effects
- Use long-acting stimulants with sustained release
  - Start with lowest dose
  - Titrate slowly
  - Evaluate symptoms/side effects every 2 weeks using ASRS
- Evaluate dosing regimen
  - Food intake
  - Time of day
  - Taking every day vs. as needed
- Ask about sleep
- Re-evaluate treatment goals

50

Stimulant Side Effects	Potential Contraindications to ADHD Pharmacotherapy*
• Dry Mouth • Appetite reduction • GI upset • Insomnia • BP & HR elevation • Dysphoria/irritability • Headaches	• Drug Hypersensitivity • Pregnancy/ Lactation • Cardiovascular disorder ◦ – Structural heart defect, arrhythmia, advanced atherosclerosis ◦ – Family history of sudden early death • Untreated hypertension (mod–severe) • Unstable substance use disorder • Unstable/Untx'd psychosis or mania • Glaucoma • Seizure or Tic disorder • Recent MAOI use (14 days)

"ADHD in Adulthood: Assessment and Pharmacotherapy", Craig Surman, Massachusetts General Hospital Adult ADHD Research Program, Harvard Medical School

***consultation, treatment, and/or monitoring may allow safe ADHD management**

Marie: Treatment Considerations

- Stimulants in pregnancy, breastfeeding
- Alternatives to stimulants
- Stimulants in context of ? Bipolar D/O
- Impact of hormonal changes on ADHD

Treatment Considerations post-partum

- Important to monitor sleep and energy
- Ask spouse/friend to help monitor for objective signs of mania
- Once finished breastfeeding, trial a LA stimulant with frequent follow-up

Marie Response to Treatment

- Marie responded very well to Concerta 45mg
- She received positive feedback at work and was given increased responsibility
- No longer behind on paperwork
- Less socially anxious
- Improved memory, less forgetful, not losing things
- Less need to control her environment
- Binge eating much better controlled
- Improved marital relationship
- Less overwhelmed at home and with her kids

Achieve and Maintain Functionality

- Assess functional impairment by asking about
  - Work/School
  - Family relationships
  - Social interactions

  **Weiss Functional Impairment Tool or Sheehan Disability Scale may be valuable
- Discuss and evaluate patient defined goals
- Ensure daily use of medication
- Focus on basics (sleep hygiene, routines, exercise, healthy diet, use of a planner/pda)
- Discuss coping skills development, coaching and support options (ADHD support groups, psychologist, coach)

55

Conclusions

- Adult ADHD is under-diagnosed and patients with 'red-flags' must be screened
- Comorbidity must be assessed, diagnosed and treated in order to manage the global impairment
- First line treatment of Adult ADHD should be long-acting stimulants
- Treatment must be multimodal including behaviour interventions and psychotherapy
- Treatment expectations should be discussed in the context of patient defined goals

Questions?