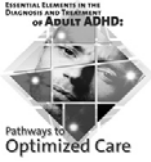


**Understanding the Challenges
in the Differential Diagnosis
of Adult ADHD**

Joel L. Young, MD

Faculty Disclosure

- **Joel L. Young, MD, is a member of the Speakers Bureau for Cephalon, Inc., Eli Lilly and Company, GlaxoSmithKline, McNeil Consumer Healthcare, Sepracor, Shire Pharmaceuticals, Inc., and Takeda Pharmaceuticals North America, Inc. He receives grants and/or research support from Cephalon, Inc., Eli Lilly and Company, and Novartis Pharmaceuticals Corporation**



Overview

- History
- Prevalence and persistence
- The economics of ADHD
- Symptom trajectory (childhood to adulthood)
- Impact on quality of life
- Functional impairments
- The diagnostic process
- Comorbidities

Historical Overview: Trajectory of Names for ADHD

- Morbid defect of moral control
- Minimal brain dysfunction
- Hyperactive child syndrome
- Hyperkinetic reaction of childhood (DSM-II)
- Attention deficit disorder with or without hyperactivity (DSM-III)
- Attention deficit/hyperactivity disorder (DSM-IV)

National Institute of Mental Health (NIMH), Attention Deficit Hyperactivity Disorder, Bethesda, Md.; NIMH, National Institutes of Health, U.S. Department of Health and Human Services

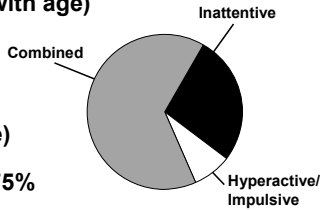
Prevalence and Persistence

- Estimated prevalence (DSM-IV-TR)
 - 6-8% of children
 - 6% of adolescents
 - 4% of adults
- Estimated 30-60% persistence into adulthood
 - ▪ Diagnosis may be residual rather than full but this is not equivalent to remission¹

¹Faraone SV, Biederman J (2005), Poster NR 458; Presented at the Annual Meeting of the APA. Atlanta; May 21-26

Prevalence of ADHD Types

- **Predominantly inattentive:**
20-30% (increasing with age)
- **Predominantly hyperactive/impulsive:** <15%
(decreasing with age)
- **Combined type:** 50-75%



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

The Economics of ADHD

- **Costs in school**
 - Special education
 - Counseling and psychological services
 - Teacher training
- **Other ADHD-related costs in childhood and adolescence**
 - Costs related to delinquency, i.e., juvenile justice system
 - Substance abuse
 - Early childbearing
 - Injury

Hinshaw S et al. (1999), Available at: www.cdc.gov. Accessed Jan. 31, 2008

The Economics of ADHD (Cont.)

- **Family costs**
 - Medical bills
 - Lost productivity
 - Accidents (vehicular and other)
- **Costs during adulthood**
 - Reduced productivity/unemployment rates
 - Behavioral issues, including: criminal activity, welfare, homelessness and substance abuse

Hinshaw S et al. (1999), Available at: www.cdc.gov. Accessed Jan. 31, 2008

Trajectory of ADHD From Childhood to Adulthood: Inattentive Symptoms

Childhood Inattentive Symptoms	Adulthood Inattentive Symptoms
Difficulty sustaining attention in school and at home (homework, chores)	Difficulty sustaining attention on the job (meetings, paperwork)
Losing items	Procrastination, difficulty budgeting time
Appears not to listen	Inefficient, slow to get things done
Trouble with follow-through	Follow-through continues to be a problem
Difficulty with organization	Disorganized

Adler LA (2004), J Clin Psychiatry 65(suppl 3):8-11; APA (1994), Diagnostic and Statistical Manual of Mental Disorders, 4th Ed. (DSM-IV), Washington, D.C.: American Psychiatric Publishing, Inc.

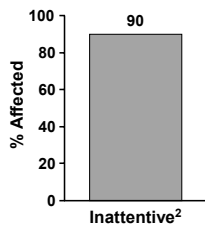
Trajectory of ADHD From Childhood to Adulthood: Hyperactive/Impulsive Symptoms

Childhood Hyperactive/Impulsive Symptoms	Adulthood Hyperactive/Impulsive Symptoms
Squirring, fidgeting, can't stay in seat	Can't sit through meetings
Can't wait turn, blurts out answers	Can't wait in line, interrupts others
Runs/climbs excessively, can't work or play quietly	Drives too fast, self-selects very active job
Intrudes, interrupts others	Makes inappropriate comments (no "mental filter")

Adler LA (2004), J Clin Psychiatry 65(suppl 3):8-11; APA (1994), Diagnostic and Statistical Manual of Mental Disorders, 4th Ed. (DSM-IV), Washington, D.C.: American Psychiatric Publishing, Inc.

Presentation of Adults: Inattentive vs. Hyperactive/Impulsive Symptoms

- Hyperactive symptoms often decline with age but inattentive symptoms do not decline substantially with age¹



N=149; p<0.05; ¹Biederman J et al. (2000), Am J Psychiatry 157:816-818; ²Millstein R et al. (1999), J Atten Disorders 2:159-166



ADHD Symptoms in Adults

Inattentive Symptoms	Hyperactive/ Impulsive Symptoms
Difficulty sustaining attention	Fidgety
Appears not to listen	Restless and jittery
Trouble with follow-through	Excessive talking
Difficulty with organization	Impatient
Easily distracted by external stimuli	Acts without thinking
Forgetful	Difficulty sitting still
Loses things often	Always "on the go"

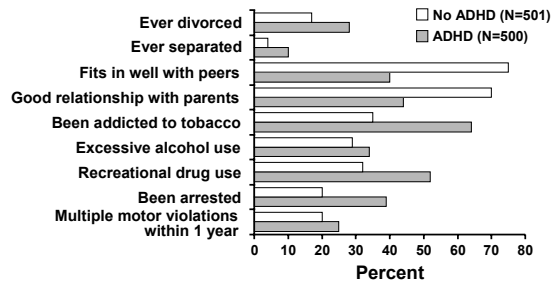
APA (1994), Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV). Washington, D.C.: American Psychiatric Publishing, Inc.

Quality of Life Issue for ADHD Adults

- ADHD symptoms may lead to¹:
 - Low self-esteem, frustration, hopelessness
 - Depression, anxiety, fatigue
 - Substance abuse (self-medication)
- Impulse dyscontrol may lead to:
 - Arguments, accidents, increased spending, legal difficulties, substance use²
 - Disappointing their partner with forgetfulness, lack of follow-through²
 - Divorce rates are higher (28% of those with ADHD have been divorced, compared to 15% of controls)³

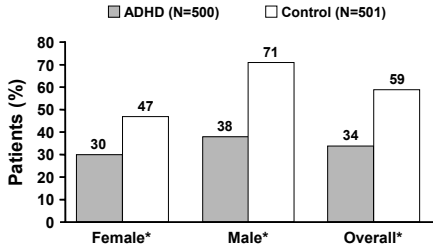
¹Young JL (2007), ADHD Grownup: Evaluation, diagnosis and treatment of adolescents and adults. WW Norton, Ltd.: London; ²Weiss M, Murray C (2003), CMAJ 168:715-722; ³Biederman J et al. (2006), J Clin Psychiatry 67:524-540

A Controlled Study of Functional Impairment



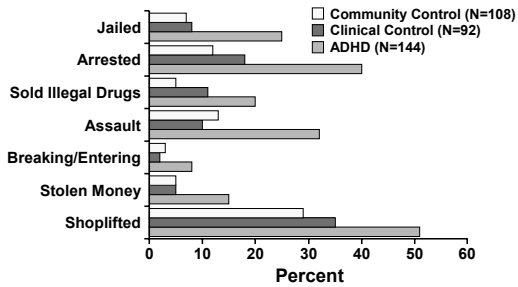
Biederman J et al. (2006), J Clin Psychiatry 67(4):524-540

Rate of Full-Time Employment in a Survey of ADHD and Non-ADHD Adults



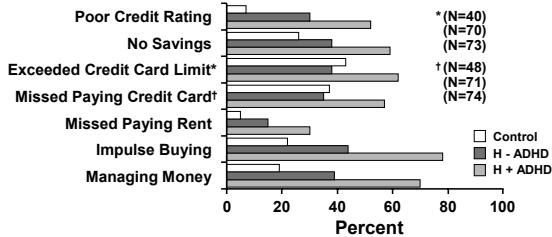
*p<0.001 for all comparisons; Biederman J et al. (2006), J Clin Psychiatry 67(4):524-540; Available at www.medscape.com. Accessed Jan. 30, 2008

Criminal Activities: ADHD, Clinical, Community



Barkley RA et al. (2008), ADHD in Adults: What the Science Says. The Guilford Press: New York

Money Management Problems in Adults With ADHD: Barkley's Milwaukee Study



H+ ADHD = hyperactive group that currently has a diagnosis of ADHD at follow-up (N=55); H-ADHD = hyperactive group that does not have a diagnosis of ADHD at follow-up (N=80); Control = sample from community (N=75)

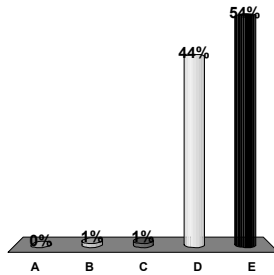
Barkley RA et al. (2008), ADHD in Adults: What the Science Says. The Guilford Press: New York



Keypad Question

The diagnosis of adult ADHD is complicated by which of the following:

- A. Hypothyroidism
- B. Hyperthyroidism
- C. Iron deficiency anemia
- D. Bipolar disorder
- ✓ E. All of the above



Symptom Assessment Scales

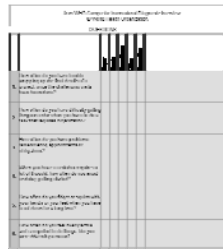
Examples

- Brown ADD Scale
- Conners Adult ADHD Rating Scale
- Adult Self-Report Scale (18-item version and 6-item version: 6-item is a good tool for ruling out the diagnosis in general client population)
- ADHD module

Adler LA (2004), J Clin Psychiatry 65(suppl 3):8-11

Example of a “Symptom Assessment Scale”

- The Adult Self-Report Scale (ASRS) is predictive **but not diagnostic**; often a good place to start the process



ASRS: World Health Organization; Adler LA (2004), J Clin Psychiatry 65(suppl 3):8-11

The Clinical Interview

Timeline of Symptoms

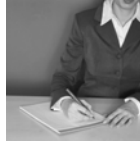
- When did these symptoms first appear?
- What were you like as a child, both in school and at home? (Report cards can be helpful here; look at grades and citizenship marks)
- Have the symptoms been chronic or episodic?
- How have these symptoms affected your functioning?

Young JL (2007), ADHD Grown Up: A Guide to Adolescent and Adult ADHD, W.W. Norton

The Clinical Interview

Reason for Presentation and Goals for Treatment

- What is bringing you in today?
- Why now?
- Did someone recommend that you seek treatment? If so, who?
- How can we be helpful to you?



Young JL (2007), ADHD Grown Up: A Guide to Adolescent and Adult ADHD, W.W. Norton

The Clinical Interview

- Family history
 - Be sure to include patient's children in the history; the diagnosis is often made this way
- Clinical observations
 - Does the patient have a hard time sitting still?
 - Do the patient's thoughts quickly shift from one topic to another?
 - Is the patient talking excessively?
 - Does the patient often lose his train of thought?
 - Is the patient late to the appointment or disorganized upon arrival?

Young JL (2007), ADHD Grown Up: A Guide to Adolescent and Adult ADHD, W.W. Norton

The Clinical Interview: Challenges in Differential Diagnosis of Adult ADHD

Consider Medical Rule-Outs

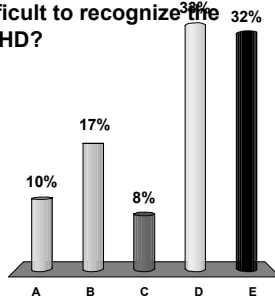
- **Thyroid disorders**
 - Hypothyroidism: may exhibit inattentive symptoms
 - Hyperthyroidism: may exhibit hyperactivity and inattention, act impulsively
- **Iron deficiency anemia**
 - Inattention
 - Slowed cognitive processes
- **Consider comorbidities**

Young JL (2007), ADHD Grown Up: A Guide to Adolescent and Adult ADHD, W.W. Norton

Keypad Question

Which of the following similarities between ADHD and bipolar disorder make it difficult to recognize the differential diagnosis of ADHD?

- A. No psychosis present
- B. Mood swings are rapid and brief but not severe
- C. Symptoms are episodic
- D. Mood swings are present
- E. Symptoms are chronic



Challenges in Differential Diagnosis of Adult ADHD: Symptom Overlap

Hyperactivity/Impulsivity	Bipolar Mania
Similarities	Similarities
Excessive talking	Excessive talking
"On the go"	"On the go"
Often acts without thinking	Often acts without thinking
Racing thoughts	Racing thoughts
Mood swings	Mood swings
Differences	Differences
Symptoms are chronic	Symptoms are episodic
No psychosis present	Typically accompanied by psychosis
Mood swings are rapid and brief but not severe	Mood swings last from days to weeks and can be severe

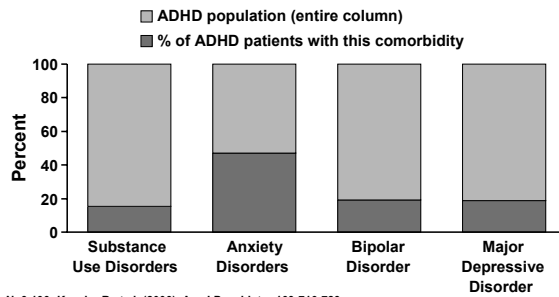
Young JL (2007), ADHD Grown Up: A Guide to Adolescent and Adult ADHD, W.W. Norton

Challenges in Differential Diagnosis of Adult ADHD: Symptom Overlap

ADHD-Related Frustration	Depression
Frustrated by underperformance	Hopelessness, helplessness, suicidality
Symptoms are chronic	Symptoms are episodic
Minimally relieved by antidepressants	Generally responsive to antidepressants
Often triggered by an event	Onset can occur with or without a trigger
Amotivation	Psychomotor retardation

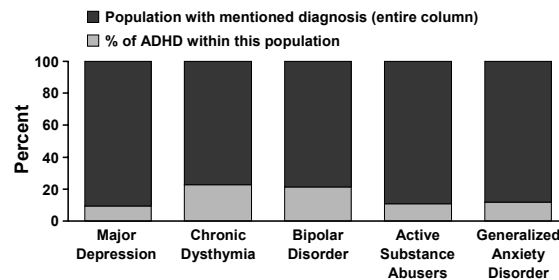
Young JL (2007), ADHD Grown Up: A Guide to Adolescent and Adult ADHD, W.W. Norton

Comorbidity: Other Psychiatric Disorders Within the Universe of ADHD



N=3,199; Kessler R et al. (2006), Am J Psychiatry 163:716-723

Comorbidity: ADHD Within the Universe of Psychiatric Disorders



N=3,199; Kessler R et al. (2006), Am J Psychiatry 163:716-723



Conclusions

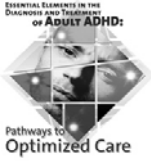
- ADHD symptoms in adults can lead to:
 - Low self-esteem, frustration, hopelessness
 - Depression, anxiety, fatigue
 - Substance abuse (self-medication)
 - Functional impairments and quality-of-life issues
- Diagnosis is a multifaceted process
- Carefully consider comorbidities and medical rule-outs

Evaluating Treatment Strategies for Adult ADHD

Michael A. Schwartz, MD

Faculty Disclosure

- Michael A. Schwartz, MD, has been a member of the Speakers Bureau for AstraZeneca, Eli Lilly and Company, Cephalon, Inc., Pfizer Inc., Takeda, and Wyeth Pharmaceuticals



Adult ADHD

- How, when and what to treat?
- Practice guidelines exist for child patients with ADHD (AAP)
 - Diagnosis and evaluation of the child with ADHD¹
 - Treatment of the school-aged child with ADHD²
- There are no corresponding practice guidelines for adults with ADHD³

¹Committee on Quality Improvement, Subcommittee on ADHD (2000), Pediatrics 105(5):1158-1170;
²Committee on Quality Improvement, Subcommittee on ADHD (2001), Pediatrics 108(4):1033-1044; 3NIMH. ADHD. Available at: www.nimh.nih.gov/health/publications/adhd/complete-publication.shtml#pub8. Accessed September 30, 2008

Adult ADHD: Treatment Principles

- Individualize treatment plans
- A highly heterogeneous disorder. Prevalence 4.4%
 - Most patients untreated or treated for comorbidity¹
- ADHD persists into adulthood in 10-60% of documented child cases²
 - Less hyperactivity, more restlessness and irritability
 - Inattentiveness predominates along with social difficulties and deterioration of executive functioning
- High rates of comorbidity (77%) exist in adulthood³

¹Kessler RC et al. (2006), Am J Psychiatry 163:716-723; ²Marks DJ et al. (2006), Ann NYAS 931:216-383; Kadesjo B, Ginsberg C (2001), J Child Psychol Psychiatry 42(4):487-492

High Comorbidity in Adult ADHD ...

- ~~Represents independent diagnostic entities~~
- Reflects desperate genetic/environmental underpinnings
- Subtypes of a central ADHD syndrome
- "ADHD" is an early precursor/manifestation of comorbidity
- Developmental coupling
 - Presence of 1 syndrome heightens risk for other
- Phenomena is an artifact of greater impairment at time of assessment

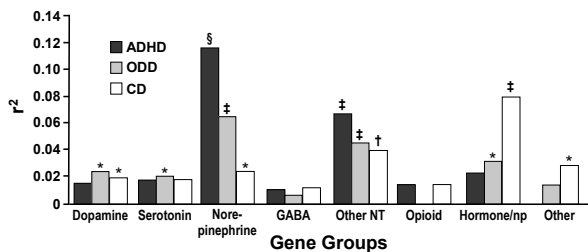
Marks DJ et al. (2006), Ann NYAS 931:216-38

Comorbidity and Adult ADHD

- **Alcohol misuse** 32-55%^{1, 2, 4, 5}
- **Other substance use disorders** 8-32%^{1-3, 5, 6}
- **Mood disorders** 19-35%^{1-3, 6}
- **Anxiety disorders** 25-50%^{1-3, 6}
- **Learning disorders** 9-94%(children)⁶
- **Antisocial behavior** 18-28%^{1-3, 6}
- **Other personality disorders** 10-20%^{1, 3, 6}

¹Biederman J et al. (1993), Am J Psychiatry 150:1792-1798; ²Shekim WE et al. (1990), Compr Psychiatry 3:416-25; ³Mannuzza S et al. (1993), Arch Gen Psych 50:565-576; ⁴Murphy K et al. (1996), Compr Psychiatry 37(6):393-401; ⁵Roy-Byrne P et al. (1997), Compr Psychiatry 1997;38:133-40; ⁶Marks DJ et al. (2006), Ann NYAS 931:216-38

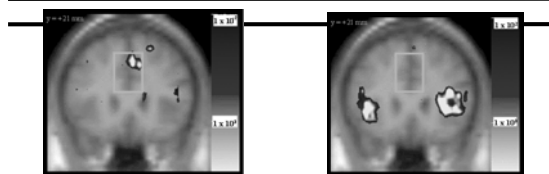
Heterogenous Genetics Cumulative Value for Eight Different Groups of 42 Genes



- **Genetic diversity: characteristic of entities such as height and weight (all subjects comorbid)**

*p<0.05; †p<0.01; ‡p<0.005; §p<0.001; Comings DE et al. (2000), Clin Genet 58(1):31-40

Adult ADHD: fMRI



Normal Control

ADHD

- **The anterior cingulate cognitive division (ACCd) plays a central role in attentional processing**
- **ADHD subjects fail to activate the ACCd during an attentional/cognitive interference task (Stroop test)**

Bush G et al. (1999), Biol Psychiatry 45:1542-1552

**Adult ADHD Nonpharmacological Treatment:
Cognitive-Behavioral Therapy (CBT)**

- Insight-oriented therapy not shown effective
- CBT introduced as a feasible, next-step treatment approach for residual symptoms^{1, 2}
- Meta-Cognitive Therapy (MCT)
 - Manualized group cognitive-behavioral therapy extends principles of CBT to development of executive self-management skills³

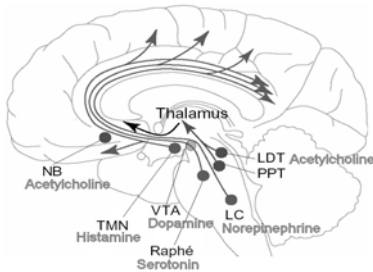
¹Safren SA et al. (2005), Behavior Research and Therapy 43(7):831-842; ²Safren SA et al. (2005), Mastering Your Adult ADHD: A Cognitive-Behavioral Treatment Program Client Workbook. Oxford; ³Soltano MV et al. (2008), J Attention Disorders 11(6):728-736

Adult ADHD Nonpharmacological Treatment

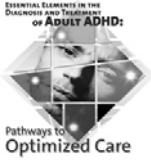
- Psychoeducation, counseling, supportive problem-directed therapy, and coaching¹⁻³
 - Relaxation training and stress management
 - Behavioral coaching to teach strategies for organizing home and work activities
 - Job coaching or mentoring to support better working relationships and improve on-the-job performance
 - Family education and therapy
- Neurofeedback a possible viable alternative/complementary treatment with improvement documented objectively and subjectively⁴

¹Wender PH et al. (2001), Annals NY Acad of Sciences. Available at: <http://www3.interscience.wiley.com/journal/120754232/abstract>. Accessed September 30, 2008; ²Wilens T et al. (2004), JAMA 292:619-623; ³Swartz SL et al. (2005), Psychology in the Schools 42(6):647-56; ⁴Lubar JF et al. (2005), Applied Psychophysiology Biofeedback 30(4):366-373; Fox DJ et al. (1995), Applied Psychophysiology Biofeedback 20(1):83-99; Monstra V (2005), Child and Adolescent Psych Clinics North America 14(1):55-82

**Adult ADHD Pharmacotherapy: Mechanism of Action: Effect on Networks of Neurotransmitters
(Mediate Factors Such as BDNF)**



Saper CB et al. (2001), Trends Neurosci 24:726-731; Chen MJ et al. (2007), Cellular Signalling 19(1):114-128



Range of FDA Approved Medication Options for ADHD

- **Stimulants**
 - **Short-acting**
 - Methylphenidate and amphetamine preparations
 - **Long-acting**
 - Methylphenidate and amphetamine preparations
 - Prodrug: lisdexamfetamine (Vyvanse)
- **Non-stimulant (Norepinephrine reuptake inhibitor)**
 - Atomoxetine

Range of Medication Options With RCT in Children or Adults

- **Antidepressants¹**
 - Amitriptyline (Elavil)
 - Bupropion (Wellbutrin)
 - Desipramine (Norpramin)
 - Imipramine (Tofranil)
- **α-agents¹**
 - Clonidine (Catapres)
 - Guanfacine
- **MAOIs**
- **Dopaminergic agent²**
 - Modafinil (Provigil)

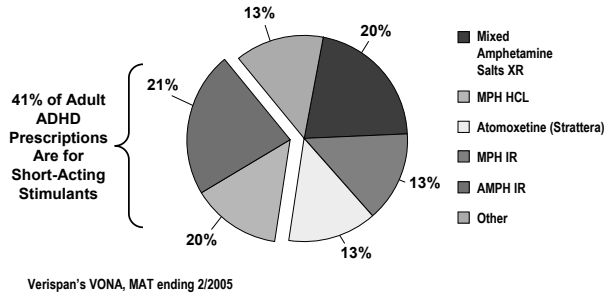
¹Ordway G et al. Brain Norepinephrine Cambridge 2007; ²Swanson JM et al. J Clin Psychiatry 2006 67(1):137-147

Stimulants: General Principles

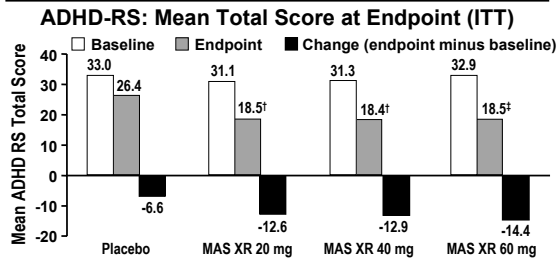
- **Stimulants are gradually titrated**
 - IR medication may be mixed with extended-release
- **Patients will respond to stimulants in a markedly individualized manner**
- **Responses can also vary symptom by symptom (e.g., hyperactivity may respond more than inattentiveness)**
- **Each symptom and clinical problem should be tracked separately**

Spencer T et al. (1996), J Am Acad Child Adolesc Psychiatry 35:409-432

Short-Acting Stimulants: Share of Adult Prescriptions



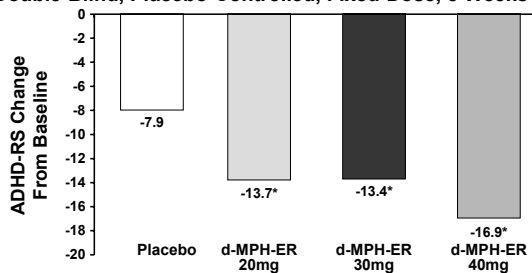
MAS XR Study in Adult ADHD: 4-Week, Double-Blind, Placebo-Controlled, Forced Titration Dose* (N=255)



MAS XR = mixed amphetamine salts extended release; *Daily dose = 20, 40, 60 mg (adjusted Dunnett test compared with placebo after ANCOVA with baseline score as covariate); †p<0.05; ‡p<0.001; Weisler RH et al. (2006), CNS Spectr 11(8):625-639

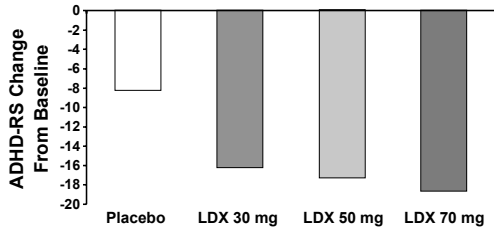
Dexmethylphenidate Extended-Release (d-MPH-ER) Efficacy in Adults

Double-Blind, Placebo-Controlled, Fixed-Dose, 5 Weeks (N=221)



*p<0.01; Spencer TJ, Adler L (2007), Biol Psychiatry 61(12):1380-1387

Efficacy of Lisdexamfetamine (LDX) in Adult ADHD

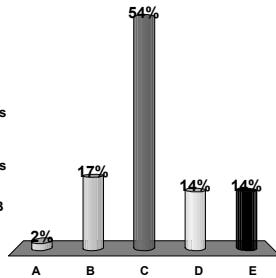


Adler L et al. (2007), Poster presented at the 54th Annual Meeting of the American Academy of Child and Adolescent Psychiatry; Boston; October 25

Keypad Question

Which of the following is correct regarding medications for adult ADHD?

- A. Stimulants are recommended for use in patients with glaucoma or taking MAOIs
- B. Stimulants may exacerbate hypothyroidism and increase seizure threshold
- ✓ C. Norepinephrine reuptake inhibition increases dopamine in the prefrontal cortex but not other brain regions such as the nucleus accumbens or the striatum
- D. Norepinephrine reuptake inhibition decreases dopamine in the prefrontal cortex but not other brain regions such as the nucleus accumbens or the striatum
- E. Amphetamine, methylphenidate and atomoxetine are all pregnancy category B



Stimulant Tolerability and Safety

- ~~Monitor heart rate and BP after every dose increase in patients with cardiac risk factors~~
 - MI, stroke and sudden death reported with all stimulants
- Exacerbation of OCD, insomnia, anorexia and weight loss, rebound, irritability, sadness, anxiety
- Exacerbation of psychosis, precipitation of mania, lowering of seizure threshold, hypothyroidism, leucopenia (periodic CBC indicated), tics
- Not recommended in glaucoma or with MAOIs
- Drug interactions possible



Do Stimulants for ADHD Lead to Substance Abuse?

- **2 major studies of long-term outcome published in American Journal of Psychiatry in 2008**
- **“Evidence that current clinical practice does not increase later substance use or abuse is comforting, but the failure to document that childhood treatment with stimulant medication decreases the high risk of substance abuse in adulthood (45%) is distressing.”***

*Volkow ND, Swanson JM (2008), Am J Psychiatry 165:553-555; Biederman J et al. (2008), Am J Psychiatry 165:597-603; Mannuzza S et al. (2008), Am J Psychiatry 165:604-609

Side Effects With Stimulant Medication

- | | |
|--|--|
| <ul style="list-style-type: none"> • Insomnia • GI upset • Decreased appetite • Weight loss • Headaches • Dry mouth • Constipation • Hand tremors • Jittery | <ul style="list-style-type: none"> • Research on individual stimulants has generally shown no dose relationship with side-effects in group data^{1, 2} • Some research has shown side-effects may be more likely in stimulant naïve patients³ |
|--|--|

¹Weisler RH et al. (2006), CNS Spectr 11(8):625-639; ²Adler L et al. (2005), Presented at the 158th Meeting of the American Psychiatric Association, May 21-25; ³Goodman DW et al. (2005), CNS Spectr 10(Suppl 20):26-34

Patients Risks–ADHD Medication Diversion

- **List of the 20 most diverted prescription medications, according to a 13-year summary of crime statistics published by the city of Cincinnati¹**
 - Dextroamphetamines were ranked #14
 - Methylphenidate
- **Reports of methylphenidate and amphetamine misuse/abuse among adolescents and young adults are particularly disturbing²**
 - **Laura Nagel, Deputy Assistant Administrator; Office of Diversion Control, US Drug Enforcement Agency**

¹Top Prescription Drugs Diverted October 1, 1990-July 21, 2003. Cincinnati Police Division Squad. PO Box 141257. Cincinnati, Ohio 45250. ²Drug Enforcement Administration. Available at: www.deadiversion.usdoj.gov/pubs/brochures/stimulant/stimulant_abuse.htm. Accessed February 25, 2005

Selective Norepinephrine Reuptake Inhibitor (NRI)

- Atomoxetine
 - Once-daily dosing
 - No evidence of abuse potential
 - May take 4-6 weeks to see full effect
 - Long-term sustained effect shown in clinical trials (Adult studies up to 34 weeks) Improvement sustained in studies, with further 43.5% reduction in Conners Adult ADHD scale*

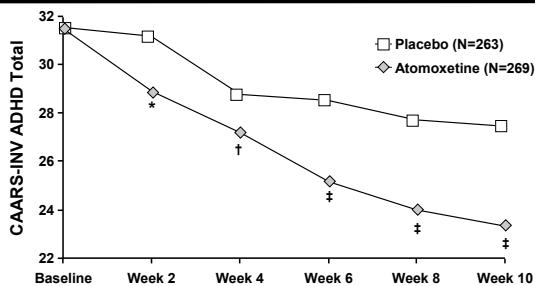
*Simpson D, Plosker GL (2004), Drugs 64 (2):205-222

Role of NE Reuptake Inhibition on DA is Focal and Selective

- Norepinephrine reuptake inhibition increases DA in the prefrontal cortex but not other brain regions such as the nucleus accumbens or the striatum^{1, 2}
- Avoiding increases in striatal and NA dopamine may spare patients tics, euphoria and addiction
- Alternatively, patients with aimlessness, lack of motivation and drive may need increased dopaminergic activity in the locus coeruleus

¹Yamamoto BK, Novotney S (1998), J Neurochem 71:274-80; ²Bymaster FP et al. (2002), Neuropsychopharmacology 27:699-711

Atomoxetine in Adult ADHD: Pooled Data From 2 DBPC Studies



*p<0.003; †p<0.05; ‡p<0.001; DBPC = double-blind placebo-controlled; CAARS-INV = Conners' Adult Attention Rating Scale, Investigator Rated; Michelson D et al. (2003), Biol Psychiatry 53(2):112-120

Atomoxetine in Adult ADHD: Side Effects

Side Effect	Atomoxetine (%)	Placebo (%)
Dry mouth	21	7
Insomnia	21	9
Nausea	12	5
Decreased appetite	12	3
Decreased libido	7	2
Erectile difficulty	10	1
Dizziness	6	2

Increased BP (systolic, diastolic): 1 to 3 mm Hg

Increased HR: 5 bpm

All significant vs. placebo; Michelson D et al. (2003), Biol Psychiatry 53(2):112-120

Atomoxetine Tolerability and Safety

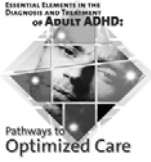
- Increased risk of suicidal thinking and behavior in children and adolescents
- Use cautiously in patients with hypertension, tachycardia and CV or cerebrovascular disease
- Risk of hypotension in patients so disposed
- Caution in patients with liver dysfunction
- Not recommended in narrow angle glaucoma or with MAOIs

www.fda.gov

Pregnancy and Breastfeeding

- ~~Amphetamines, methylphenidate, atomoxetine~~ all pregnancy Category C
 - Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks
- Amphetamine and methylphenidate are detectable in breast milk
 - American Academy of Pediatrics considers amphetamines and methylphenidate a contraindication for breastfeeding

Spigset O et al. Am J Psychiatry 2007;164(2):348; Hackett LP et al. Ann Pharmacother 2006;40(10):1890-1891; Illett KF et al. Br J Clin Pharmacol 2007;63(3):371-375



Numerous Medications Are in Development for ADHD

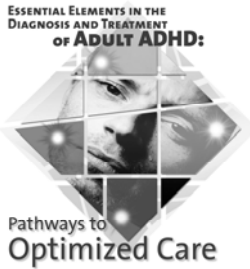
- 335 studies are listed as of 10/1/08 at: www.clinicaltrials.gov
- Novel studies involve nicotinic and histaminergic receptors
- Various drug delivery systems are being investigated
- Non-pharmaceutical treatments are being investigated

www.clinicaltrials.gov. Accessed September, 2008

Conclusions

- Increasing medication options-stimulant and non-stimulant are available or being investigated for adults with ADHD
- Psychotherapeutic approaches add additional benefits to treatment outcomes
- Concurrent psychiatric comorbidity needs to be assessed, prioritized and considered in treatment planning

Question-and-Answer Session



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