Management of ADHD

Dr Henal Shah
Professor (Addl),
TNMC & BYL Nair Ch. Hospital

Epidemiology: ADHD

- Most commonly diagnosed behavioral disorder of childhood (1 in 20 worldwide)
- 3 – 7% of school children are affected in U.S.,
- Males:Females = 2 – 9:1
- Girls less hyperactivity, fewer conduct problems, & less externalizing behavio

Epidemiology

- A gender paradox
  - *lower* prevalence will show a *more severe* clinical presentation, along with severity/greater levels of comorbidity (Loeber & Keenan, 1994)
  - Consistent with multifactorial/polygenic conditions:

Epidemiology

- At least 70% maintain diagnosis during adolescence
- At least 50% maintain diagnosis during adulthood

- Strongest predictor of poor prognosis i[illegible] pubertal aggression

Why More ADHD?

- Improved recognition by physicians?
- Increase in prevalence?
- An easing of standards for making the diagnosis?
- An easing of standards for prescribing medication?...
- Increased scholastic demands?
- Changing parental habits?
- Managed care and the pharmaceutical industry?

Case I Anushka

8 years old
Younger sibling

Brought by tired parents
with behaviour
and scholastic problems

History

- Normal antenatal period
- Caesarian section due to prolonged labour
- Social and motor milestones normal
- Slight delay in speech development

Problems

- Never sitting still
- Badgering the mother, talkative
- Constantly playing with water
- All things perpetually scattered everywhere
- Falling and hurting self on multiple occasions
- Fearless, got lost in mall and entertainment park
- Not paying attention whilst studying
- Not listening to instructions, forgetful
- Not writing in class, never doing HW

Deepika mom n dad g’parents

Family History

- Suicide in maasi
- ? Depression in maternal grandpa
- ?substance abuse in mama
- Dil-Mil problems; separation of bil

- On probing mother depressed
- Father perfectionist
- Leading to fights between the two

Solutions

- What is your diagnosis of Anushka?
- How will you manage the case?
- Mother believes in counseling and homeopathy and is not for allopathy
- Father wants to know whether she will always be like this?

Clinical Picture

- Inattentiveness: style of behaviour involving disorganisation and lack of persistence

(rather than psychological processes indexed by tests for attention)

- Overactivity:

(excess of movement)

Impulsiveness

(acting without reflection)

Hyperactivity

Attention Deficit Hyperactive Disorder

Must meet **at least 6** of the criteria within A1 and/or A2, and have experienced for at least the past 6 months.

A1: Inattention

A2: Hyperactivity and Impulsivity

Attention deficit without hyperactivity

Responsible for cognitive impairment: working memory, poor spatial skills, delay in language, motor coordination IQ often lowered

Check if secondary

Taylor& Sonuga Barke, 2007

B. Several inattentive or hyperactive-impulsive symptoms were present prior to age 12.

C. Criteria for the disorder are met in two or more settings (e.g., at home, school or work, with friends or relatives, or in other activities).

D. There must be clear evidence that the symptoms interfere with or reduce the quality of social, academic, or occupational functioning.

E. The symptoms do not occur exclusively during the course of schizophrenia or another psychotic disorder and are not better accounted for by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, or a personality disorder).

Typical presentation: Inattention

Preschool	Primary school	Adolescence	Adulthood
•Short play sequences (<3min) •Leaving activities incomplete •Not listening	• Brief activities (<10min) •Premature change of activity •Forgetful, disorganised, distracted	•Persistence less than peers (<30min) •Lack of focus on details •Poor planning ahead	•Details not completed •Appointments forgotten •Lack of foresight

Disorders of attention and activity:Taylor and Sonuga Barke, Rutter, 2008

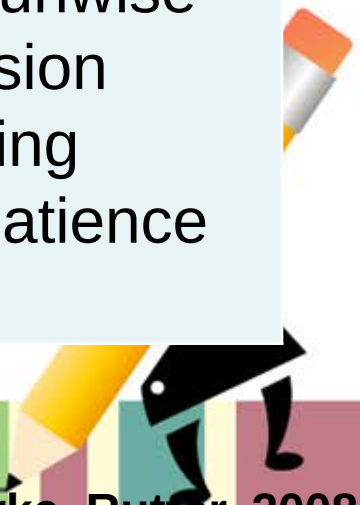
Typical presentation: Overactive

Preschool	Primary school	Adolescence	Adulthood
•whirlwind	•Restless when calm expected	•Fidgety	•Subjective sense of restlessness

Disorders of attention and activity:Taylor and Sonuga Barke, Rutter, 2008

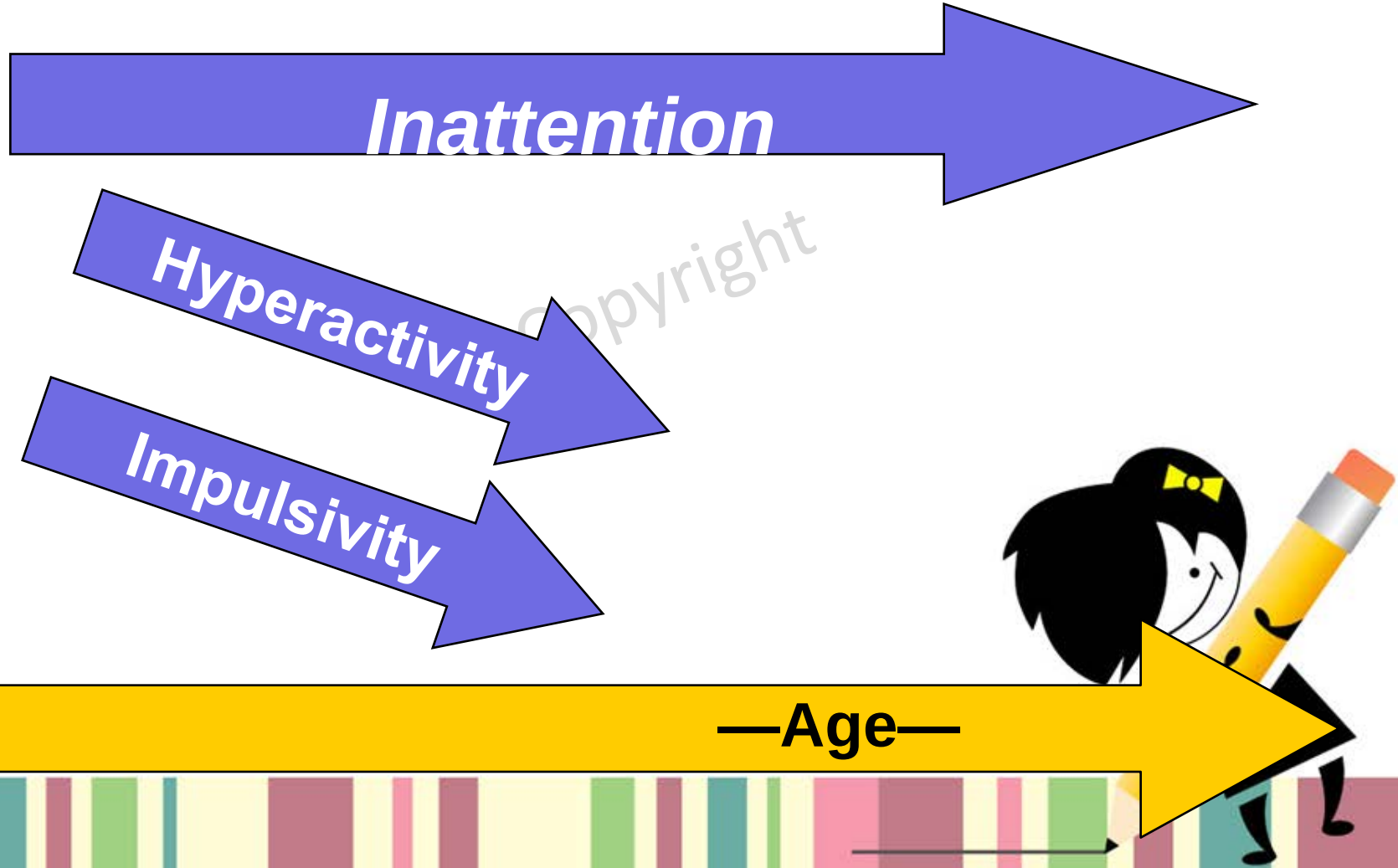
Typical presentation: Impulsive

Preschool	Primary school	Adolescence	Adulthood
•Does not listen •No sense of danger (oppositionality)	•Out of turn •Interrupting •Thoughtless rule breaking •Intrusion on peers •Accidents	•Poor self control •Reckless risk taking	•Motor and other accidents •Premature and unwise decision making •Impatience



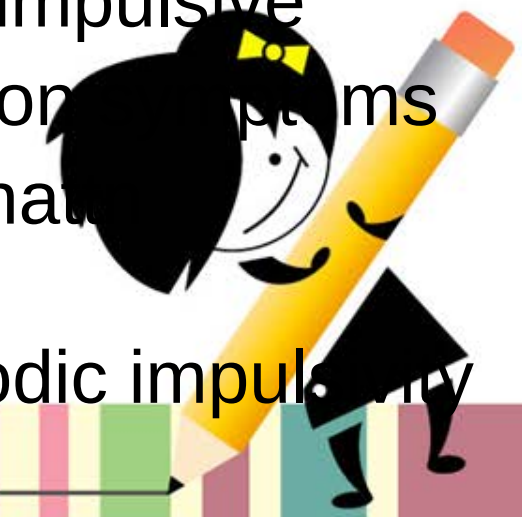
Disorders of attention and activity:Taylor and Sonuga Barke, Rutter, 2008

ADHD: Course of the Disorder



Natural History

- Rule of “thirds”:
  - 1/3 ➔ complete resolution
  - 1/3 ➔ continued inattention, some impulsivity
  - 1/3 ➔ early ODD/CD, poor academic achievement, substance abuse, antisocial adults
- Age related changes:
  - Preschool (3-5 y/o) – hyperactive/impulsive
  - School age (6-12 y/o) – combination
  - Adolescence (13-18 y/o) – more inat
    w/restlessness
  - Adult (18+) – largely inattn w/periodic impul



MTA

- Careful medication> powerful than BT

  > effective than community rx

Combination improved aggression, sense of satisfaction, possible decrease in dose and normalisation

Re analysis: hyperkinetic superior to treat with medication; ADHD but not hyperkinetic,

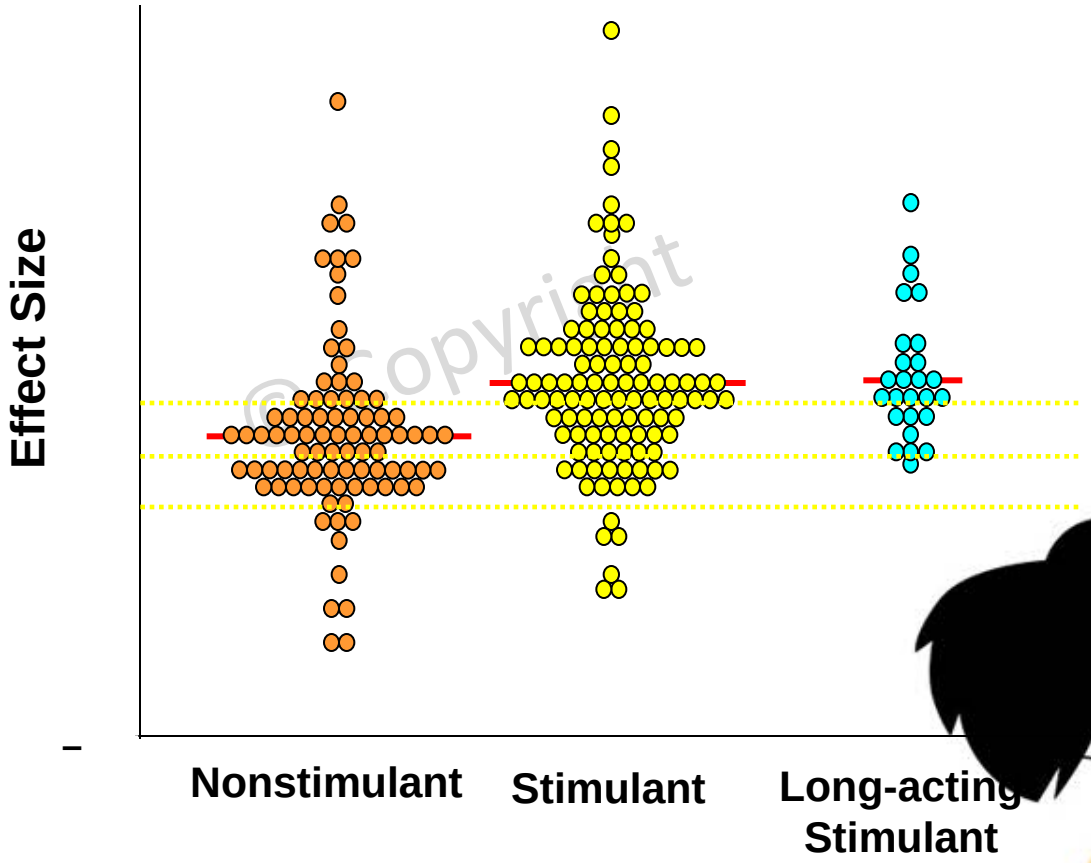
choice of therapy is balanced

MTA,1999; Santosh et al, 2005

Relative Efficacy of ADHD Therapies: Effect Size

Effect size:
a statistical measurement of the *magnitude of effect* of a treatment.

Large = 0.8
(Swanson et al, 2001)



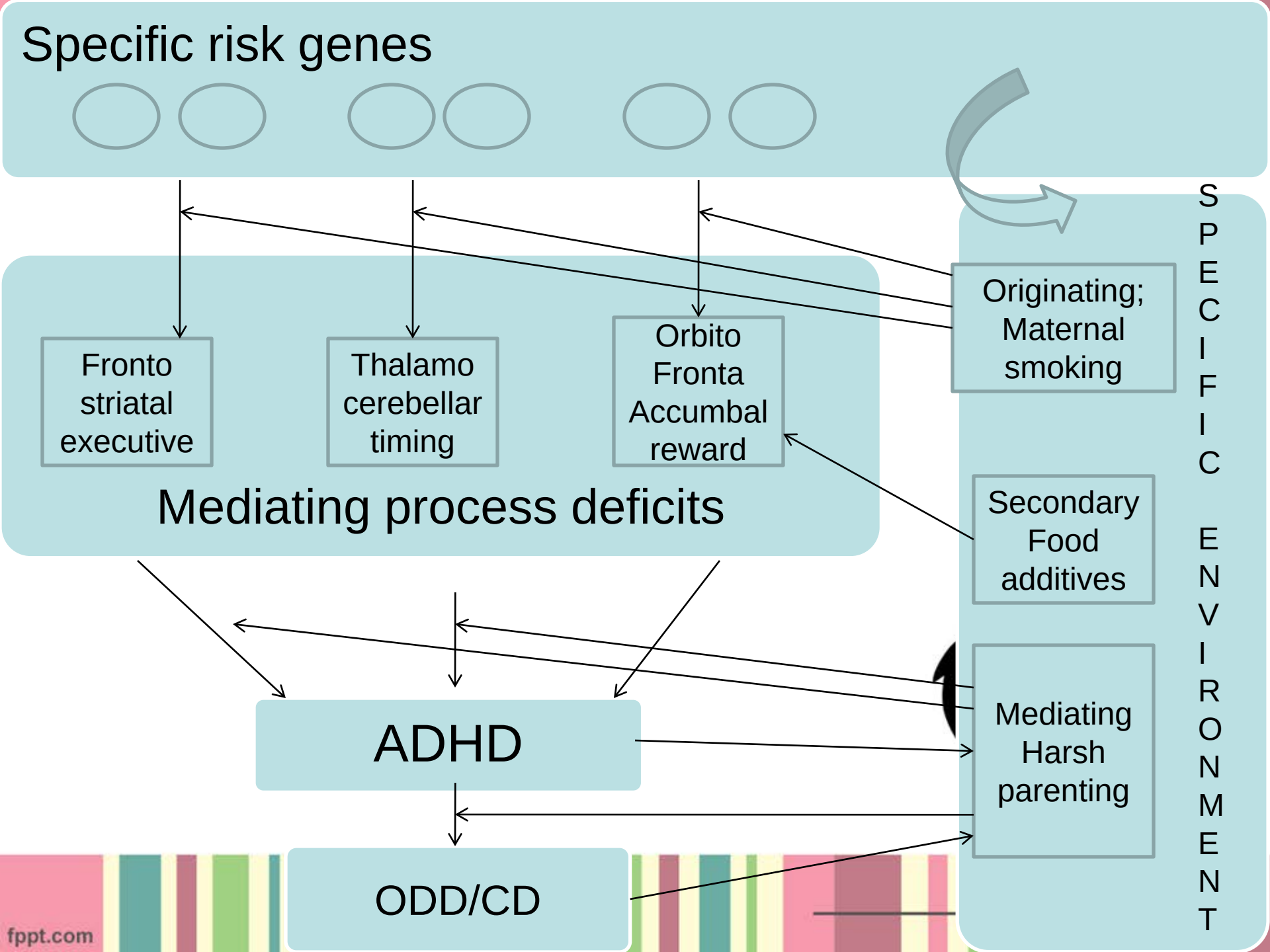
Faraone SV et al. Poster presented at APA; May 17–22, 2003; San Francisco, CA.
Swanson JM et al. *J Am Acad Child Adolesc Psychiatry*. 2001;40:168–179.

Stimulants : Dosage

- Routine PE prior to initiation of stimulants; Vitals checked periodically
- Long-acting treatments are good options given concerns about tachyphylaxis
- Dosing averages: 30 mg/d MPH

Stimulants

- Weight based dosing (not generally utilized)
  - Methylphenidate @ 0.7 -1 mg/kg
- Dose to clinical response, weekly titration
- Forced Dosage Titration
  - E.g., for a 100+ pound (.45kg) child: long acting 18 mg/d week #1; 36 mg/d week #2; and 54 mg/d week #3


Specific risk genes
Fronto striatal executive
Thalamo cerebellar timing
Orbito Fronta Accumbal reward
Mediating process deficits
Originating; Maternal smoking
Secondary Food additives
Mediating Harsh parenting
SPECIFIC ENVIRONMENT
ADHD
ODD/CD
fppt.com

Parent Problems Related to ADHD

- Parents of children w/ADHD are 3-5x more likely to become separated or divorced
- Parents of children w/ADHD have a higher incidence of depression & family discord
- Majority of parents of children w/ADHD report making changes in work status
- 9 – 35% risk that a parent of a given patient has ADHD

Case 2

Master B is a 12 year old boy who is constantly getting into trouble. His mother says that since she can remember he has been as "*driven as a motor engine"*. She had to change the interiors of her house when he was a child as he was constantly falling over things and injuring himself frequently.

His teachers frequently complain from school that he is constantly talking and disturbing others and he's one of the naughtiest boys in class. He gets punished and reprimanded frequently, and genuinely feels guilty, but seems to forget all that in a short time and again does the same things.

His parents are fed up of whacking him and his teachers are tired of punishing him. Now his academic performance particularly in languages, social studies and math has deteriorated so much,

that the principal is seriously thinking of telling his

parents to put him in a special school/or a different

curriculum.

Age: 12
Std: 7th
IQ:- 122

Worksheet

Importance of Trees

There are various types of trees in our surrounding environment. Trees are the natural ~~tree~~ thing because we get the trees from nature. Trees ~~is~~ are useful for birds in purpose of the shelter they get food from tress. In markets there great demand for the medicinal trees and tress from which cosmetics are made. We get rubber, gum and many other things from trees. Trees gave the fresh air for ~~ma~~ humanbeing. The important thing is trees gave ~~o~~ out the oxygen and ~~th~~ take the gas is a carbondioxide. But day by day man is cutting down the ~~tree~~ trees to their needs. Man is Clearing the forests for buit buildings and the factories. Save trees, save nature and save your life.

My favourite sport

My favourite sport is Cricket. Cricket is in various types. There are Test matches, One day matches, 50-50, and T20 matches. In match there are 11 players in each team. The cricket match is between two team. There is Captain, Wisecaptain, Wicketkeeper, Bowler, Batsman and Allrounders in a team. There are 3 umpires in a each match. Cricket is an excersice sport. We stay active by playing this game. An it is a outdoor ~~gam~~game. It is necessary to wear kit while playing in international matches for our safety.

Spot the errors in the sample.

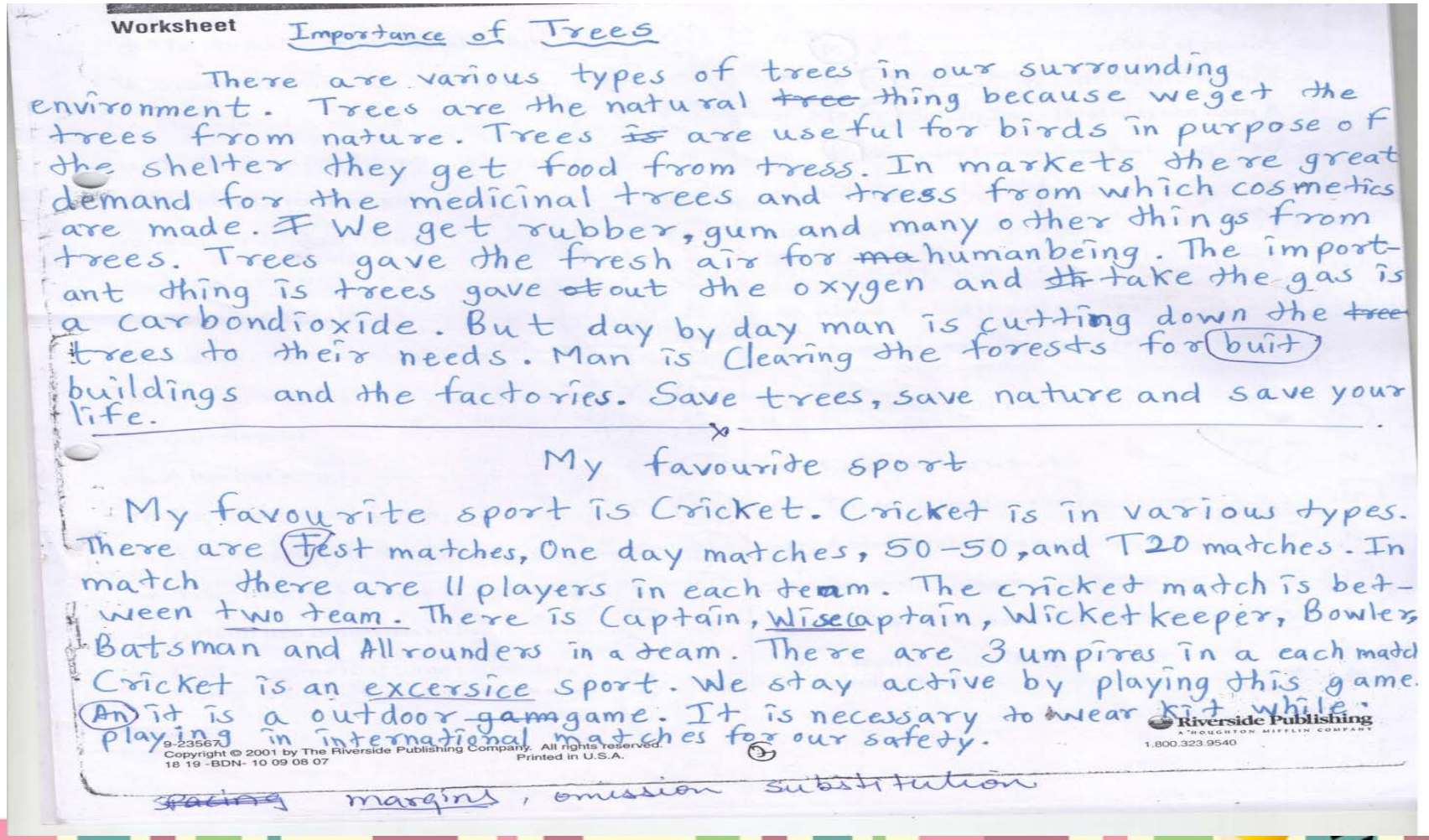
What do you think is the problem with Master B?

What would be your plan to approach the case?

What can be done to help the child?

Will shifting him to another school
be beneficial?

Age: 12
Std: 7th
IQ:- 122



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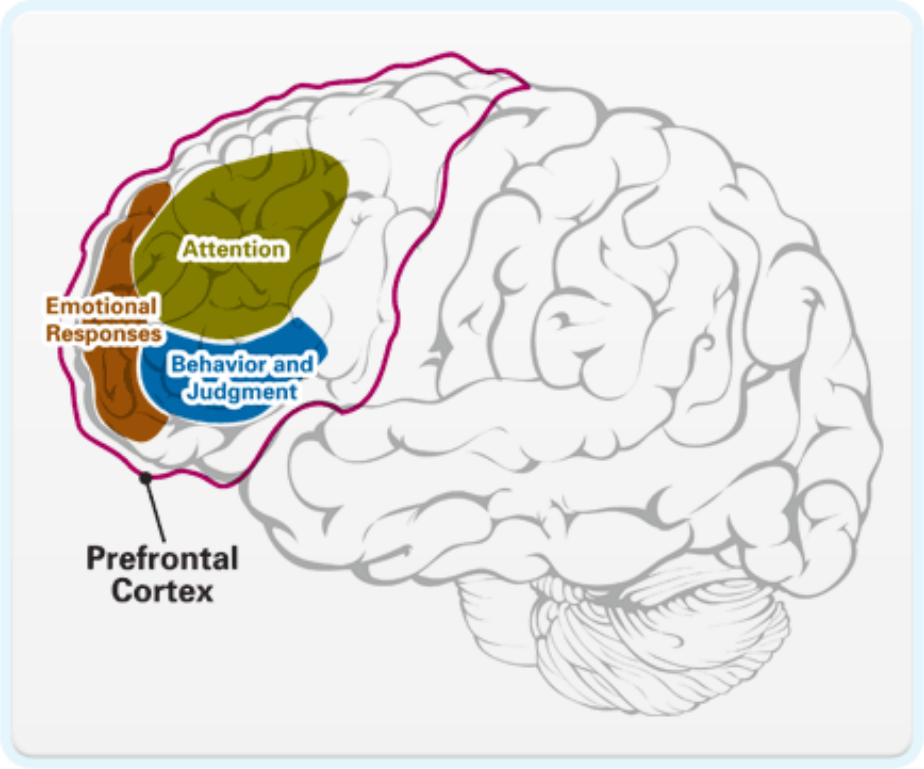
~~Pacing~~ margins, omission substitution

ADHD – Pathophysiology

Low dopamine (DA) and norepinephrine (NE) activity in the prefrontal cortex
DA affects: behavior; NE affects: attention

76% explained by heritability



ADHD Guidelines

- 4-5 yr: Behavioral therapy (CBT); stimulant 2nd line (BT not possible , worsening, weigh risks)
- 6-11 yr: Medication (MPH/ATX/Guanfacine/Clonidine)+/CBT
- 12-18 yr: Medication +/- CBT (both preferred)
- Adults: Medication +/- CBT (both preferred)
- Prior to starting medications: screen for subst abuse and diversion of medications

ADHD: Clinical Practice Guideline for the Diagnosis,Evaluation and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents, AAP, 2011

Non pharmalogical treatment

Children

- Counseling
- Behavior modification
- Education

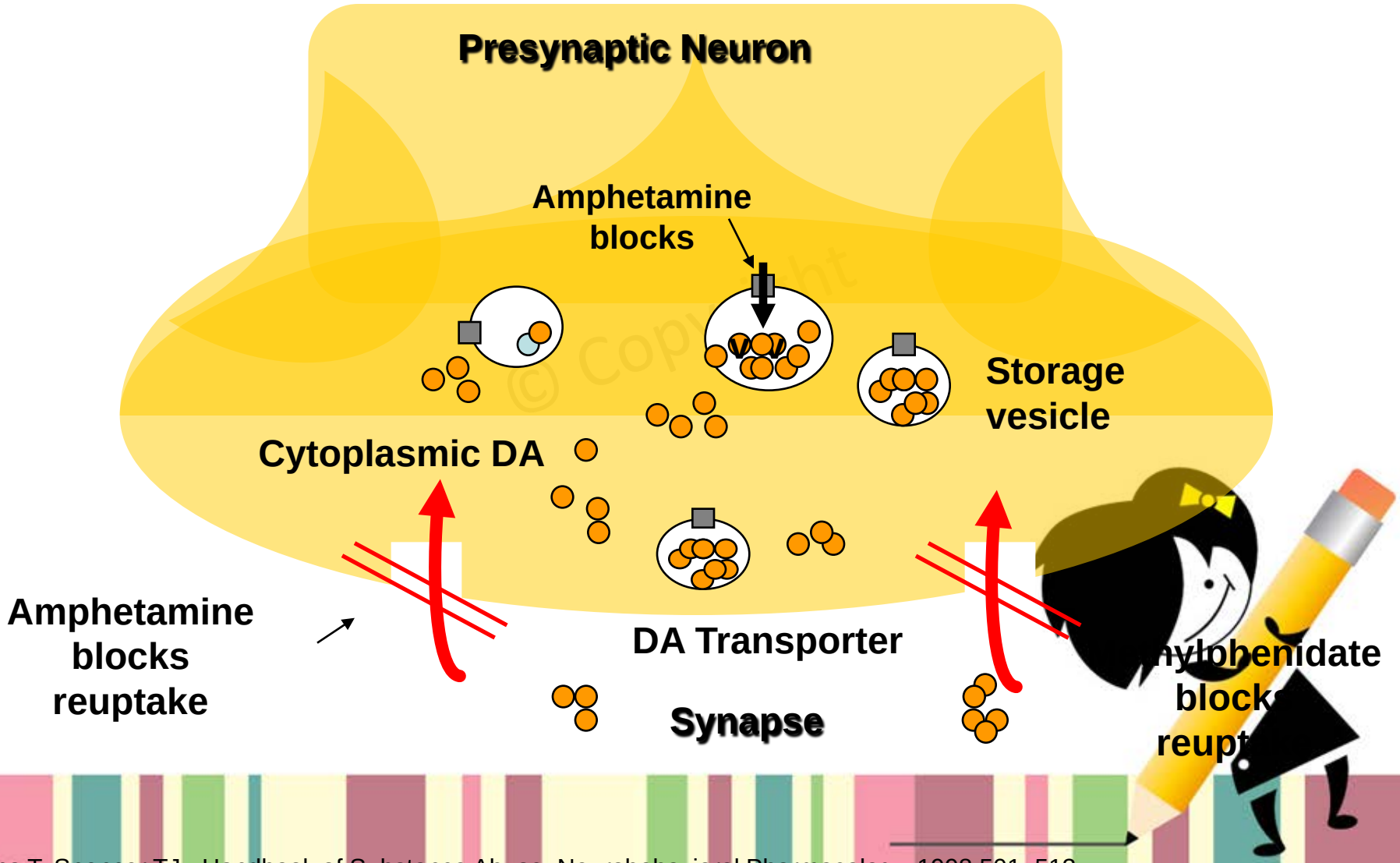
Adults

- Counseling
- Education

Stimulants: Mechanism of Action

- Reuptake inhibition of NE & DA
- Cause increased release of presynaptic NE/DA
- Methylphenidate are mild inhibitors of MAO

Mechanism of Action of Stimulants



Wilens T, Spencer TJ. Handbook of Substance Abuse: Neurobehavioral Pharmacology. 1998;501–513

Stimulants : Response Rates

- 70% response rate w/a single stimulant (DEX/MPH); 90% respond if both tried

- Behavioral rebound

- 6 of 8 studies in preschool age (3 - 6 y/o)
  found MPH effective;
  no studies w/ADD & DEX (paradoxically approved for preschool children)

Consider Stimulants

- History of favorable response to stimulants
- Those who require “drug holidays”
- Obese/overweight patients
- Concern about manic activation
- Augmenting Atomoxetine
- When you need a “powerful punch”
- Any newly diagnosed patient for whom
  determine the treatment to be appropr

Consider Atomoxetine

- History of adverse effect to stimulants
- Comorbid anxiety, depression, tics, enuresis or Tourette's
- Require 24 hour symptom relief
- Severe stimulant rebound
- Personal or family history of substance abuse
- Concern about insomnia or appetite suppression
- Monthly prescriptions are a major hassle
- Any newly diagnosed patient for whom you determine the treatment to be appropriate

Stimulants : Standard Care

Routine Treatment with Stimulants and Atomoxetine

Prior to treatment

- Height, weight, Blood Pressure & Heart Rate
- Cardiac Exam
- Family history of sudden cardiac death and/or personal or family history of syncope, chest pain, shortness of breath, or exercise intolerance warrants an ECG and pediatric cardiology referral for an echo

During Treatment

- At least annual height & weight (compare to published norms); if height for age decreases by > 1 standard deviation while on stimulants, refer to a pediatric endocrinologist (re: possible growth hormone deficiency or hypothyroidism)
- Repeat blood pressure and heart rate at least twice annually and anytime prior and subsequent to a dosage increase

Stimulants Contraindications

- Contraindications: HTN,
- symptomatic cardiovascular disease,
- glaucoma,
- hyperthyroidism,
- tics/Tourette's (relative),
- drug abuse (relative),
- psychosis (relative)

Atomoxetine: Mechanism

- Norepinephrine reuptake inhibitor; acts at presynaptic neuron; primary mechanism
- Significant increase in dopamine noted in PFC
- No DA increase noted in nucleus accumbens (limbic system)
- No DA increase noted in striatum

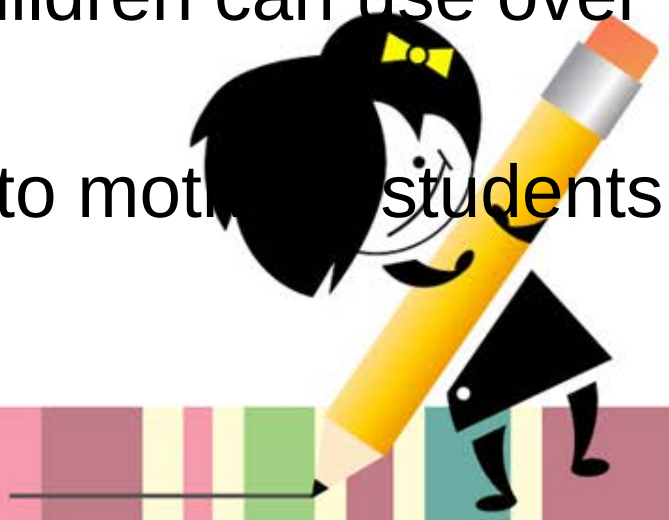
Long Term Effects on Academic Success

- 18 year study of >5,000 children from birth found treatment with stimulants is associated with improved long-term academic success.
- Untreated ADHD (both gender) were equally vulnerable to poor school outcomes.
- By age 13, on average, stimulant dose was modestly correlated with improved reading achievement scores.
- Treatment was associated with decreased absenteeism.
- Children with ADHD who were treated with stimulants were 1.8 times less likely to be retained a grade than children with ADHD who were not treated.

Barbaresi et al. 2008

Organizational Skills Training

- Manualized Treatment, Flexibly Applied to Individual Needs
- 20 sessions conducted in 10 weeks
- Meet with child and parents
- Consult with teachers
- Focus on practical routines that children can use over and over again
- Rewards and reinforcement used to motivate students to change



Organizational Skills Management

- Tracking Assignments
- Organization of Settings
- Materials Management
  - Collection
  - Storage
  - Transfer
- Time Management
  - Time Estimation
  - Scheduling
- Planning
  - Single Time Period
  - Long-Term Projects
  - Setting Priorities
  - Determining Breaks

Coexistent disorders

- Neurodevelopmental: ASD, ID, Tourette's
- Association with other childhood onset: ODD, CD, anxiety
- Adult type: substance misuse, Bipolar disorder, schizophrenia

Case 3

Kalki is a fifteen year old girl who did not want to appear for her Board exams and therefore attempted to jump in front of the train while going to school one day.

You being the school counselor, go back to review her school records and notice that she was a brilliant child till the age of about 10 years. Following this her academic grades started dropping and every year she would score less and less. Her handwriting was bad and she really couldn't complete her work.

From a confident, bubbly child she has become quiet, with drawn lean and constantly nervous and cranky. Her mother says she is always studying and worried about her results, but she scores so badly. She hardly has any friends whom she confides in.

What do you think has happened to Kalki?

What would be your plan to approach the case?

What emotional aspects must you be vigilant of?

What would be the further plan of action academically as well as emotionally

Worksheet

Happiest day of My life

X

The happiest day of My life was the day I celebrated my 10th birthday. It is not very clear in my memory as it was 5 years ago. I had been very excited and had been planning my birthday party for days. The guests the food and the games that would be played I was accompanied by friends and family both In the celebration of my birthday. We played a lot of games and the food was delicious that was told by my guests. I cut the cake and everybody sang for me. I recived a lot of amazing gifts that day. I thanked everybody for joining me on my birthday as they left. I had a lot of fun that day.

The American Academy of Pediatrics guideline for the diagnosis, evaluation, and treatment of ADHD in children and adolescents recognizes the role of the psychostimulants, atomoxetine, and the alpha2-adrenergic agonists in the management of patients with ADHD.44 Other agents (e.g., venlafaxine, monoamine oxidase inhibitors) have been studied for the potential management of ADHD symptoms; however, these options are not currently FDA-indicated for the condition or suggested for use within the major guidelines.

- ADHD with Depression:
  1. Non-medication alternatives
  2. If ADHD worse, begin ADHD algorithm
  3. If depression worse, begin MDD algorithm
  4. If ADHD improves but there is no change in depression, begin MDD algorithm
  5. If ADHD or MDD worsens, begin MDD algorithm
  6. If MDD improves but ADHD remains unchanged or worsens, begin ADHD algorithm

- ADHD with Anxiety:
  1. Atomoxetine or Stimulant for ADHD
  2. If ADHD symptoms improve but not anxiety, add an SSRI
  3. If ADHD symptoms don't improve or anxiety persists, change to alternate ADHD agent (atomoxetine or stimulant)

- ADHD with Tics:
  1. Begin ADHD algorithm
  2. If nonresponse to ADHD treatment, continue with algorithm
  3. If ADHD improves but tics persist or worsen, add alpha-2 agonist
  4. If tics do not respond, try an atypical antipsychotic
  5. If tics do not respond, try haloperic pimozide

- ADHD with Aggression:
    1. Begin ADHD algorithm
    2. Add behavioral intervention
    3. Add atypical antipsychotic to stimulant
    4. Add LiCO3 or VPA to stimulant
    5. Use alternate agent not tried in Step #4

Table 3. Management of ADHD Medication Side Effects[59,60]

Medication	Side Effect	Strategies to Manage
Psychostimulants: side effects common to the class	Decreased appetite, nausea, vomiting, headache	Administer medication with food/after meal or switch to short-acting agent. Monitor height and weight every 6 months. Drug holidays may be beneficial if significant decrease in growth is noted.
	Sleep disturbances	Avoid late afternoon and evening dosage. Use short-acting agent or switch to atomoxetine. Decrease bedtime stimuli and consider addition of melatonin.
	Labile mood, irritability	Decrease dose or consider discontinuation of medication with further evaluation of potential comorbid conditions.
	Psychiatric symptoms	Evaluate comorbid conditions *before* starting therapy. Development of symptoms is rare (<0.1%); however, if new psychiatric symptoms emerge once a psychostimulant is started, consider changing therapy.
	Tic disorder	ADHD is a common comorbidity with tic disorders. Although ADHD medications do not cause tics, in some cases they may exacerbate an underlying tic disorder. Alternative therapies for ADHD should be considered, if tics worsen while on psychostimulants include alpha$_2$ agonists or atomoxetine.
	Cardiovascular risk	Baseline evaluation of BP, HR, and family/patient history of heart disease should occur. There is a possible increased risk of cardiovascular event when decreasing psychostimulant dose[60]; however, further investigation is needed.
	Priapism	May occur while on therapy, but has been reported after discontinuation of therapy. This is considered a medical emergency and should be treated immediately.

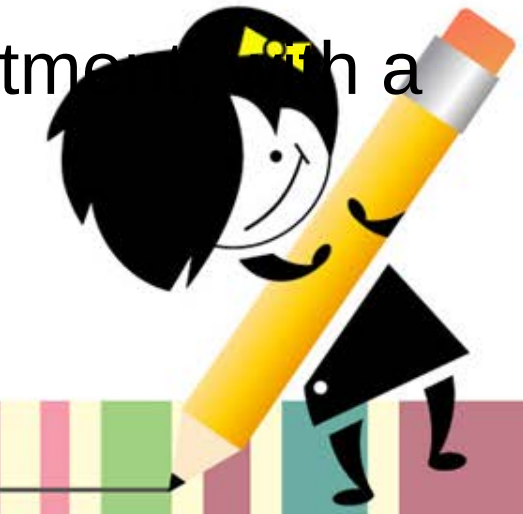
Food: high fat may affect

Atomoxetine	Abdominal pain, vomiting, decreased appetite	To assist with tolerance, use recommended dose titration when initiating therapy. May give with food. Administration BID; divided dose may help decrease side effects.
	Somnolence, fatigue, dizziness	Administer once daily at bedtime.
	Priapism	Considered a medical emergency and patient should seek care immediately.
	Psychiatric symptoms, including suicidal thoughts or behaviors	Development of new psychiatric symptoms is rare (<0.2%). Suicidal ideations (0.4%) have been noted, but no completed suicides have been reported.
Alpha$_2$ agonists	Somnolence, fatigue, dizziness	Administer at bedtime.
	Blood pressure changes	Titrate slowly to maximum effective dose to avoid lowering of BP. Avoid abrupt discontinuation and taper slowly to avoid rebound hypertension.

Are Stimulants Protective?

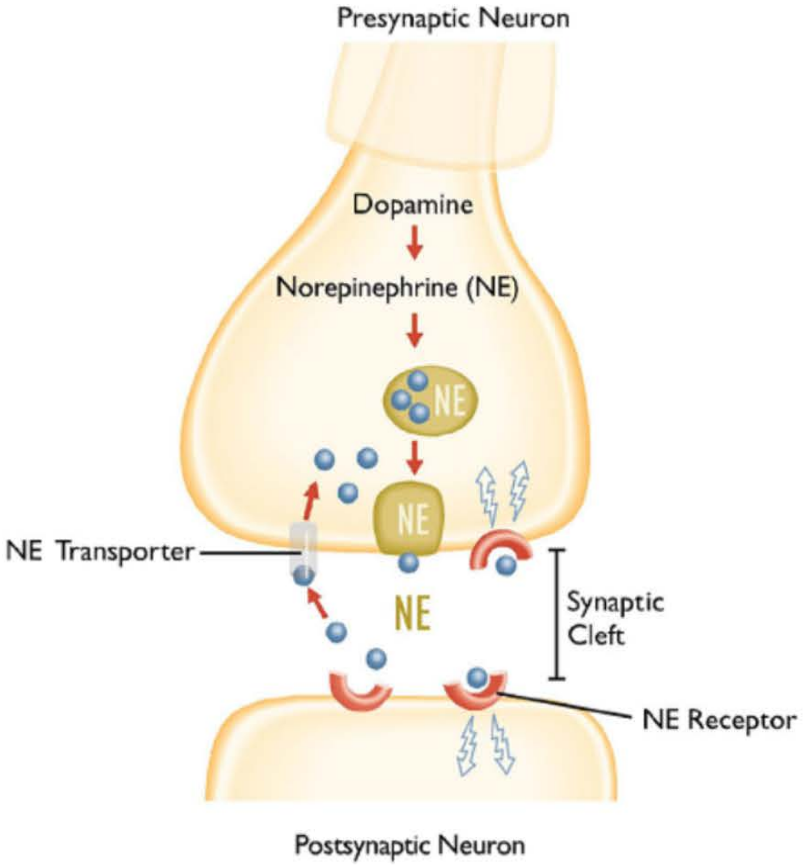
- Certainly with regard to SUDS
- 10-year, prospective study of 112 white males with ADHD ages 6 to 17 years
- 82 (73%) had received stimulant treatment with a mean treatment duration of six years

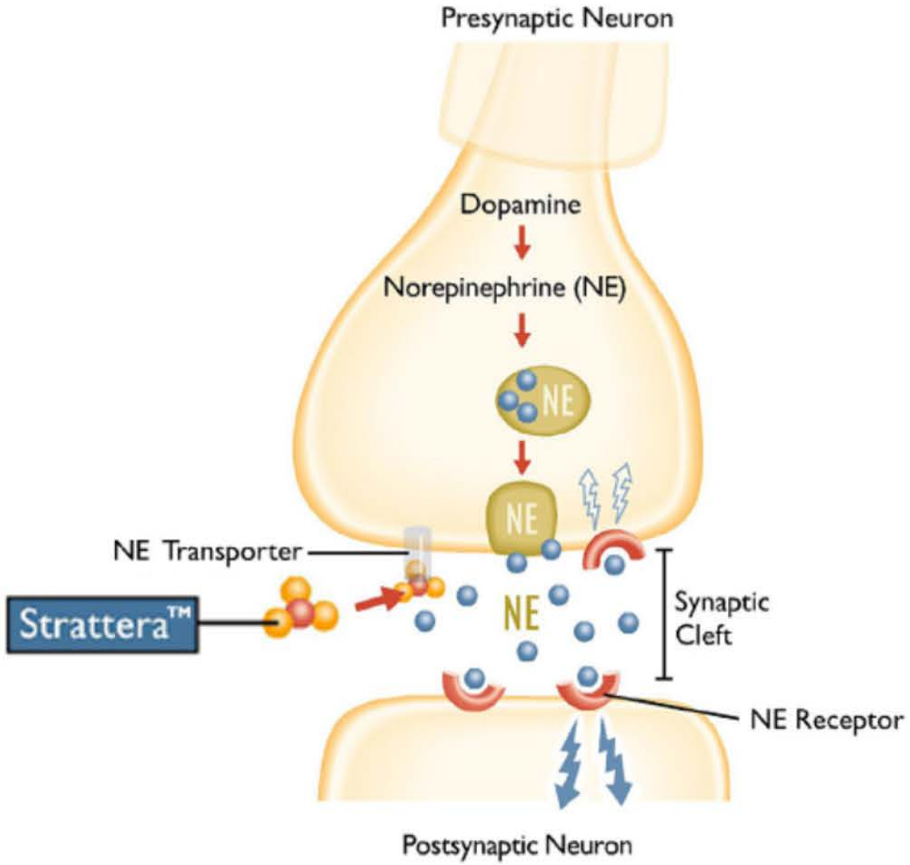
Biederman et al, 2009



Mechanism of Action

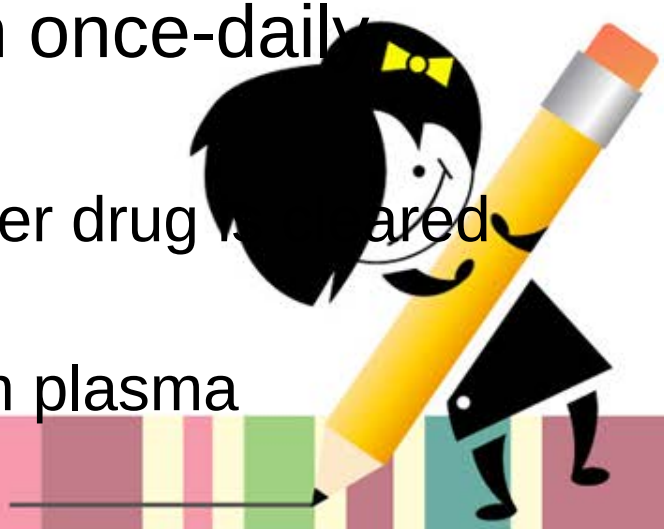
strattera™ atomoxetine HCl





Atomoxetine

- Rapidly absorbed following oral administration
- Maximal plasma concentrations reached 1–2 hrs p dose
- Metabolized via hepatic CYP P450 2D6
- Half-life ($t_{1/2}$) ~ 5 hours
  (~ 20+ hours in poor metabolizers)
- Observed duration of action with once-daily dosing suggests:
  - Therapeutic effects may persist after drug is cleared and/or
  - Brain concentration may differ from plasma concentration



Strattera: Efficacy in Children & Adolescents

- 24-hour duration of action with once-daily dosing
- Incidence of insomnia comparable with placebo (for children/adolescents)
- Not contraindicated in patients with tics and anxiety
- Nonstimulant/noncontrolled substa
- May improve some measures of functional outcome (not just core ADHD symptoms)

Strattera: Side Effects

- Children and Adolescents:
  - Decreased appetite (15%)
    - Ave wt loss of 2 – 4 LB in first 3 months, then resume nl growth
  - Dizziness (5%)
  - Dyspepsia (5%)
  - Sedation
  - BP/HR
- Adults:
  - Anticholinergic side effects (dry mouth, constipation, urinary retention)
  - Sexual SEfx (decreased libido, erectile disr[illegible], anorgasmia)
  - Insomnia
  - Nausea and decrease in appetite
  - BP/HR
- Liver Toxicity?...Suicide?

Etiology

- Genetic
- Frontostriatal/executive dysfunction
- Catecholamine disorder

Genetic

- Heretibalibity: parents & siblings 8X ↑
- Twin studies: 60-80%
- Polymorphism of D4, D5 & DATI

α-2 Agonists (1): Mechanism of Action

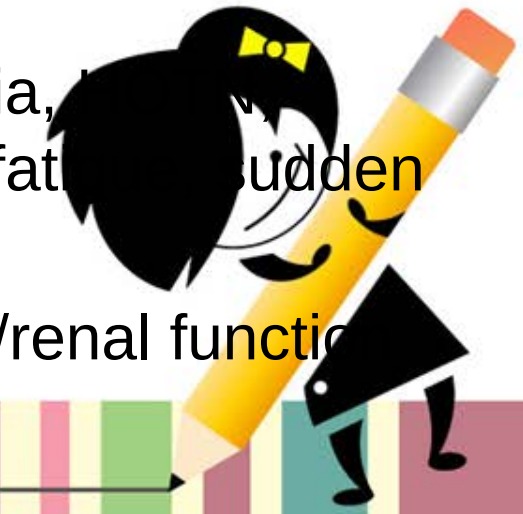
- Increased basal activity of the locus coeruleus noradrenergic cell bodies in patients with ADHD may decrease the response of the PFC
- Consequently, treatments that reduce locus coeruleus activity (e.g,. clonidine, guanfacine) have been hypothesized to improve attentional, arousal, and cognitive processes (Pliszka et al, 1996)
- Clonidine binds to the three subtypes of alpha (2) -receptors, A, B and C, whereas guanfacine binds more selectively to post-synaptic alpha (2A) - receptors, which appear to enhance prefrontal function
- Stimulation of the post-synaptic alpha-2A receptors is thought to strengthen working memory, reduce susceptibility to distraction, improve attention regulation, improve behavioral inhibition, and enhance impulse control

α-2 Agonists (2): Dosage, Treatment, and Side Effects

- Useful for residual hyperactivity & impulsivity, insomnia, treatment emergent tics, & aggression Clonidine (0.1 – 0.3 mg/d) & Guanfacine (1 – 3 mg/d)
- Routine PE/VS prior to initiation of Rx
- Contraindications: CAD, impaired liver/renal function
- Side Effects: Rebound HTN/tachycardia, SOTN, sedation, dizziness, constipation, H/A, fatigue
- Dosage: Start with HS and titrate toward morning
- Monitor BP, but ECG not routinely necessary

α-2 Agonists (5): Pros & Cons

- Clonidine (Catapres) and Guanfacine (Tenex)
- Pros:
  - Moderately effective (residual hyperactivity & impulsivity, insomnia, treatment emergent tics, & aggression)
- Cons:
  - Side Effects: Rebound HTN/tachycardia, [illegible] sedation, dizziness, constipation, H/A, fat[illegible] sudden death in combination with stimulants?
  - Contraindications: CAD, impaired liver/renal functi[illegible]



Combination Treatment

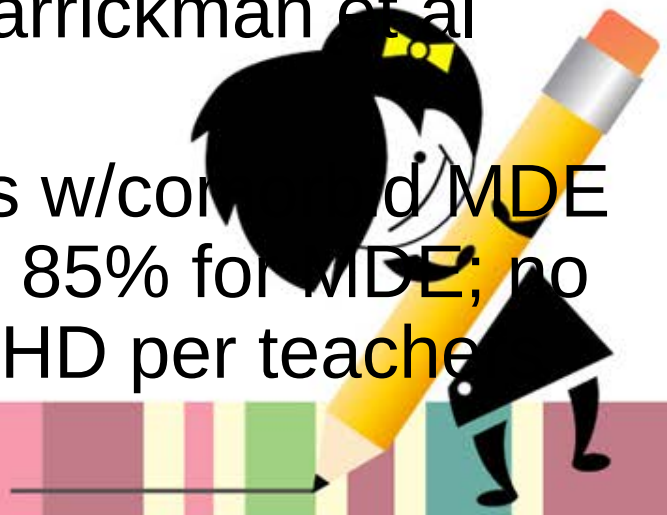
- Stimulant + α-2 Agonist:
  - Concern related to 4 reported deaths in children taking both MPH & Clonidine (each with extenuating circumstances)
  - No FDA limitations
  - AACAP recommends against routine ECGs
- Stimulant + TCA:
  - 9 deaths reported in children taking [illegible]s.
  - recent report of 10 y/o on DEX and IM[illegible] who died by cardiac arrhythmia

Tricyclics for ADHD

- DBPC trials:
  - Desipramine in adults w/68% positive responses (Wilens et al 1996, n = 41)
  - Desipramine w/comorbid tic d/o in children & adolescents (Spencer et al 2002 n = 41); 71% of pts w/ADHD responded positively; 30% decrease in tics, 42% decrease in ADHD symptoms
  - Desipramine statistically better than clonidine for ADHD with comorbid tourettes in childr[illegible] adolescents; neither exacerbated tics [illegible]er et al 1995 n = 34)
  - Desipramine in children & adolescents (Bieder[illegible]n et al 1989, n = 62); 68% responded positively "much or very much" improved

Wellbutrin for ADHD

- Adults
  - DBPC positive (Wilens et al 2001, n = 40)
  - BPP v. MPH v. placebo all negative (Kuperman et al 2001, n = 30)
- Children and Adolescents
  - DBPC positive (Conners et al 1996, n = 109)
  - BPP v. MPH both positive (Barrickman et al 1995, n = 15)
  - BPP for ADHD w/adolescents w/co[illegible]d MDE 62% response rate to ADHD, 85% for MDE; no statistical improvement in ADHD per teache (Daviss et al 2001, n = 24)

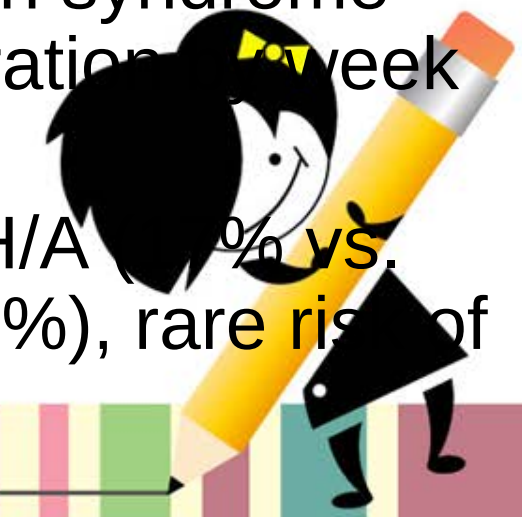


Effexor for ADHD

- Effexor - contradictory open label data in children and adults
- By example, Motavalli & Abali (2004) demonstrated efficacy in an open label study of 13 children and adolescents (average age = 10 y/o) dosed venlafaxine to an average of 40 mg (+/- 7 mg); Connors parent rating scales and CGI ratings both showed significant improvement

Modafinil (Provigil, Sparlon)

- FDA approved for narcolepsy, EDS associated with sleep apnea, & shift work sleep disorder
- Variable open label results with higher doses suggested to possibly improve symptoms of ADHD
- One RDBPC Trial, 189 children (ages 6-17), 7 weeks randomized to modafinil (dosed for weight; <30 kg = 340 mg/d & >30 kg = 425 mg/d) w/2 week blinded withdrawal (no discontinuation syndrome noted) demonstrated statistical separation [illegible] week #1 (Effect Size = 0.76)
- Side Effx = insomnia (24% vs. 1%), H/A ([illegible]% vs. 14%), decreased appetite (14% vs. 2%), rare risk of Stevens- Johnson Syndrome

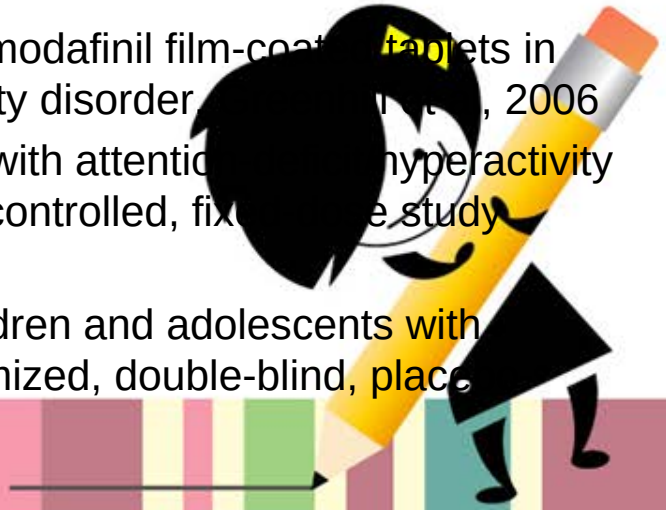


Modafinil (2): Provigil, Sparlon

- A second trial of children ages 7 – 17 with ADHD (9 weeks, double-blind, flexible dose [170 – 425 mg], randomized to once daily drug vs. placebo)
- Modafinil led to statistically significant reductions in symptoms of ADHD at home and at school
- Side Effx = insomnia, headache, decreased appetite, and weight loss

Published Modafinil Studies To Date

- A randomized, double-blind and placebo-controlled trial of modafinil in children and adolescents with attention deficit and hyperactivity disorder. Kahbazi et al, 2009
- Modafinil improves symptoms of attention-deficit/hyperactivity disorder across subtypes in children and adolescents. Biederman et al, 2008
- Modafinil as a treatment for Attention-Deficit/Hyperactivity Disorder in children and adolescents: a double blind, randomized clinical trial. Amiri et al, 2008
- Efficacy and safety of modafinil film-coated tablets in children and adolescents with or without prior stimulant treatment for attention-deficit/hyperactivity disorder: pooled analysis of 3 randomized, double-blind, placebo-controlled studies. Wigal et al, 2006
- A comparison of once-daily and divided doses of modafinil in children with attention-deficit/hyperactivity disorder: a randomized, double-blind, and placebo-controlled study. Biederman et al, 2006
- A randomized, double-blind, placebo-controlled study of modafinil film-coated tablets in children and adolescents with attention-deficit/hyperactivity disorder, 2006
- Modafinil film-coated tablets in children and adolescents with attention hyperactivity disorder: results of a randomized, double-blind, placebo-controlled, fix study followed by abrupt discontinuation. Swanson et al, 2006
- Efficacy and safety of modafinil film-coated tablets in children and adolescents with attention-deficit/hyperactivity disorder: results of a randomized, double-blind, plac controlled, flexible-dose study. Biederman et al, 2005



Vyvanse (lisdexamfetamine)

- Dextro-Amphetamine
  - Contrast to Adderall (25% L-Amp & 75% D-Amp)
- Pro-drug Stimulant (20, 30, 40, 50, 60, & 70 mg dosages)
- 10-12 hour duration
- Lower “drug liking effects” among drug abusers than amphetamine (diminishing at higher doses)
- Once daily dosing; can be dissolved in water
- Side Effx = as amphetamine

Daytrana (The “patch”)

- Methylphenidate
- 10-12 hour duration
- One patch per day worn for 9 hours
- Dosages: 10 mg (27.5 mg @ 1.1 mg/hour), 15 mg (41.3 mg @ 1.6 mg/hour), 20 mg (55 mg @ 2.2 mg/hour), & 30 mg (82.5 mg @ 3.3 mg/hour)
- Side Effx = as methylphenidate

- According to ICD 10
- **Behavioural and emotional disorders with onset usually occurring in childhood and adolescence includes**
- **Hyperkinetic disorders**

1)Disturbance of activity and attention

2)Hyperkinetic conduct disorder

3)Other hyperkinetic disorders

4)Hyperkinetic disorder, unspecified

- This group of disorders is characterized by: early onset; a combination of overactive, poorly modulated behaviour with marked inattention and lack of persistent task involvement; and pervasiveness over situations and persistence over time of these behavioural characteristics.

1)Disturbances of activity or attention includes:

- attention deficit disorder or syndrome with hyperactivity
- attention deficit hyperactivity disorder

2)Hyperkinetic conduct disorder :

- when both the overall criteria for hyperkinetic disorders and the overall criteria for conduct disorders are met.

3) Other hyperkinetic disorders

4)Hyperkinetic disorder unspecified:

- Not specific but overall criteria for hyperkinetic disorders is met.

Includes, hyperkinetic reaction or syndrome of childhood or adolescence NOS