ADHD:
An Update

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Overview

- Gain a Theoretical Framework for ADHD
- Appreciate the Current Neurobiology of ADHD
- Be Familiar with the Evaluation and Management of ADHD
- Manage ADHD, treatment refractory ADHD, and comorbidities

- ADHD: disorder of self-regulation or cognitive controls. Deficit of inhibitory control or response inhibition.

History

- 1902. Dr. George Still describes 20 children with deficits in self-control and attention span.
- 1918.Survivors of Von Economo's encephilitis have syndrome of hyperactivity and severe impulsivity.
- 1937.Dr. Charles Bradley notes Benzedrine leads to immediate improvement in self-control and attention.
- 1970. Virginia Douglas describes the cognitive dysfunction of hyperactive children.

Epidemiology

- Prevalence
  - Hyperactivity
    - 22% -57%
  - Clinical Disorder
    - 4% -6.3%
- Sex Differences
  - 3:1
- Ethnic Differences
  - US 4.4%
  - World 5.5%

Academic Impairment

- Academic Tutoring (56%)
- Repeat a Grade (30%)
- Placed in Special Education (30-40%)
- School Suspensions (46%)
- School Expulsions (10-20%)

Developmental Impairments

- **Learning Disabilities**
  - Lower IQ (avg. 10 points)
  - Reading (8-39%)
  - Spelling (12-26%)
  - Math (12-33%)
- **Language Disabilities**
  - Delayed onset by 35%
  - Speech Impairments (10-54%)
  - Delayed internalization (40%)
- **Physical Development**
  - Greater proneness to accidental injuries (57%)
  - Shorter
  - Sleep dysfunction (19%)
- **Emotional Development**
  - Teen Pregnancy (38%)
  - STDs (16%)

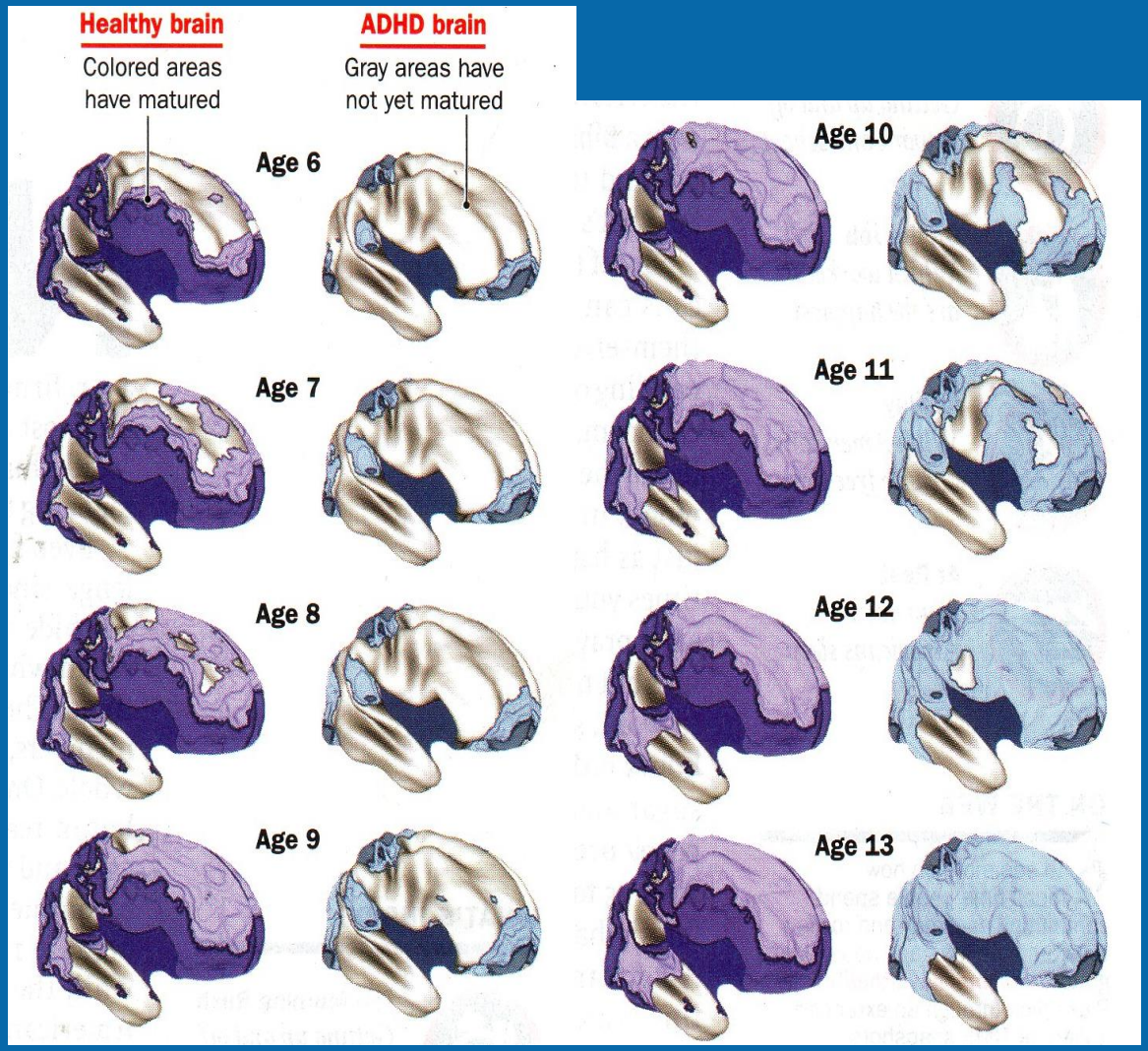
Many disorders present with similar symptoms

- **Irritability**
  - Mood disorders
  - Anxiety
  - ASD
  - Trauma
  - Environmental
  - SA
- **Poor academic performance**
  - All psychiatric disorders
  - Non-psychiatric related
  - SA
- **Inattention**
  - Mood
  - Anxiety
  - ASD
  - Sleep disorders
  - SA
  - Other Cognitive disorders such as a learning disorder
- **Hyperactivity**
  - Mood
  - SA

Etiologies; Genetic

- 35% of immediate family members of probands can be diagnosed with ADHD (Biederman et al., 1992)
- In adopted children biologic parents have higher rates of ADHD than the adoptive parents (Cantwell, 1975)
- The Concordance rate for Monozygotic twins is 100% vs. Dizygotic twins (30%) (Gilger, Pennington, and DeFries, 1992; Heffron, Martin, & Welsh, 1984)
- Heritability is 0.80
- 10-20% of non-genetic factors can be attributed to ADHD (levy et al., 1997; Nigg, 2006; Siberg et al, 2007)
- Dopamine Transporter Gene (DAT1) (Cook et al., 1997)
  - Associated with dopamine reuptake
- DRD4 gene
  - Associated with Novelty seeking behavior (Faraone et al. 1999)

Neurodevelopment



Shaw, JR et al., 2007

Diagnosis

- Persistent pattern of inattention and/or hyperactivity/impulsivity
  - More severe and frequent than others of comparable level of development
- Impairment before age 7
- Impairment in at least two settings
- Duration –six months

- Course
  - Onset
    - Hyperactivity at age 3-4
    - Combined Hyperactivity and Inattention age 5-8
    - Inattention age 8-12
  - Duration
    - 50-80% symptom continuation in adolescence
    - 40% symptom continuation in adults
  - Evolution of Symptoms

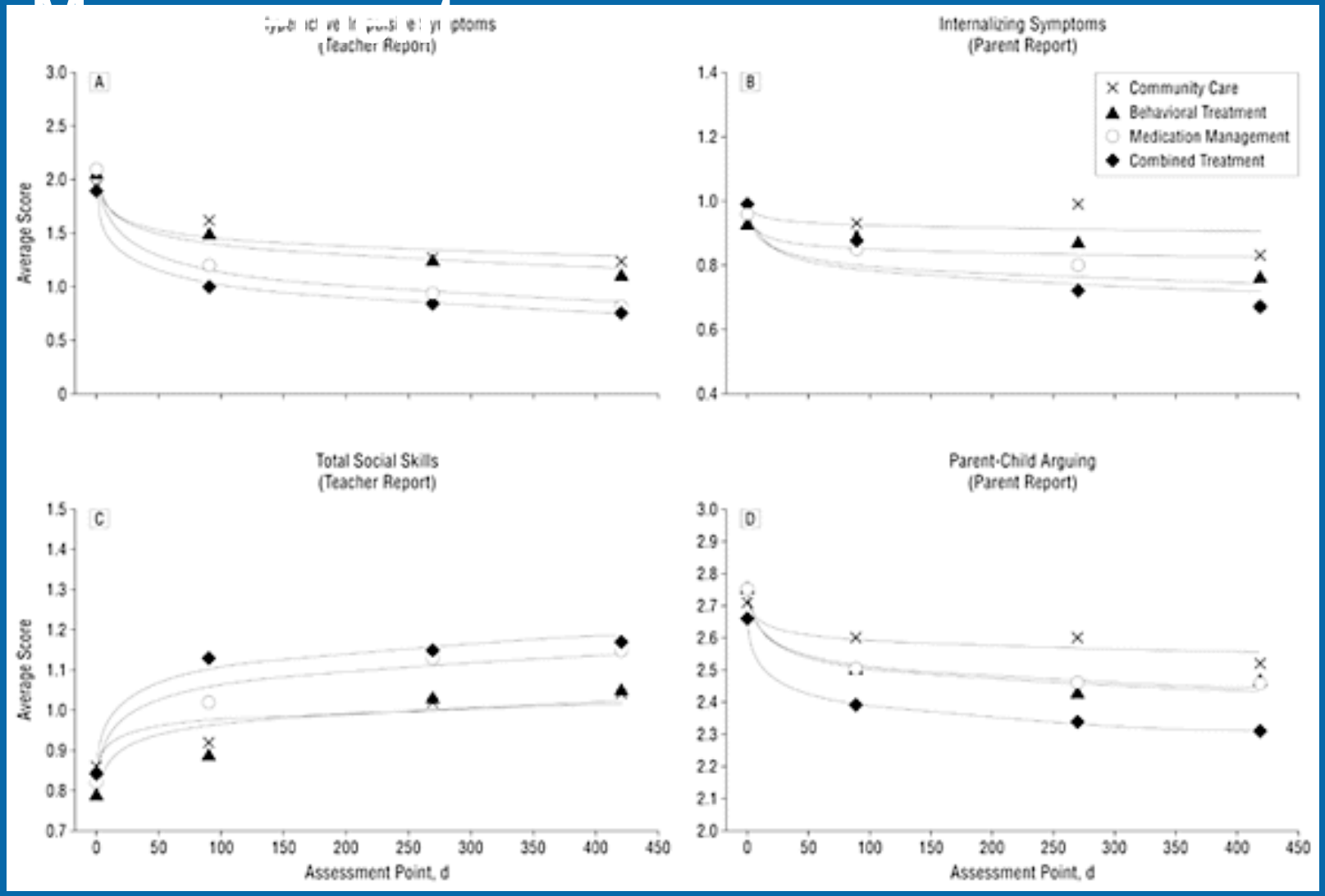
Assessment

- Clinical Interview
  - Report from parent
  - Report from another source (School)
  - Patient report
  - Medical History
  - Social History
  - Functional Impairment

- Rating Scales
  - Vanderbilt ADHD Rating Scale
  - ADHD Rating Scale
  - Conner's ADHD Rating Scale
  - CBCL

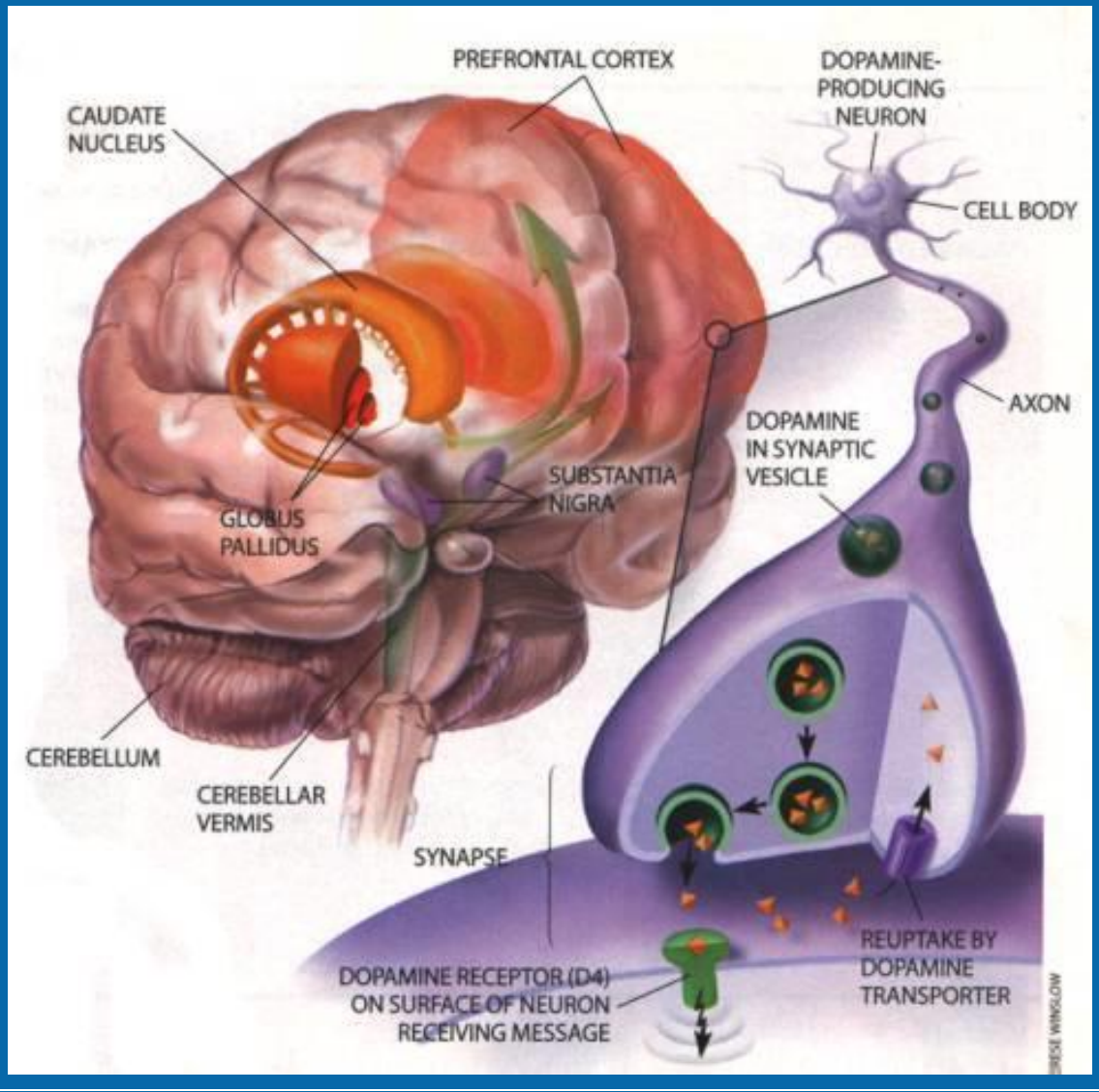
Multimodal Treatment Study (MTA)

- Government funded
- N = 579
- Ages: 7 –9.9
- Duration: 14 months
- Four groups:
  - Medication Management (MM)
  - Intensive behavioral treatment
  - Combined
  - Standard community care



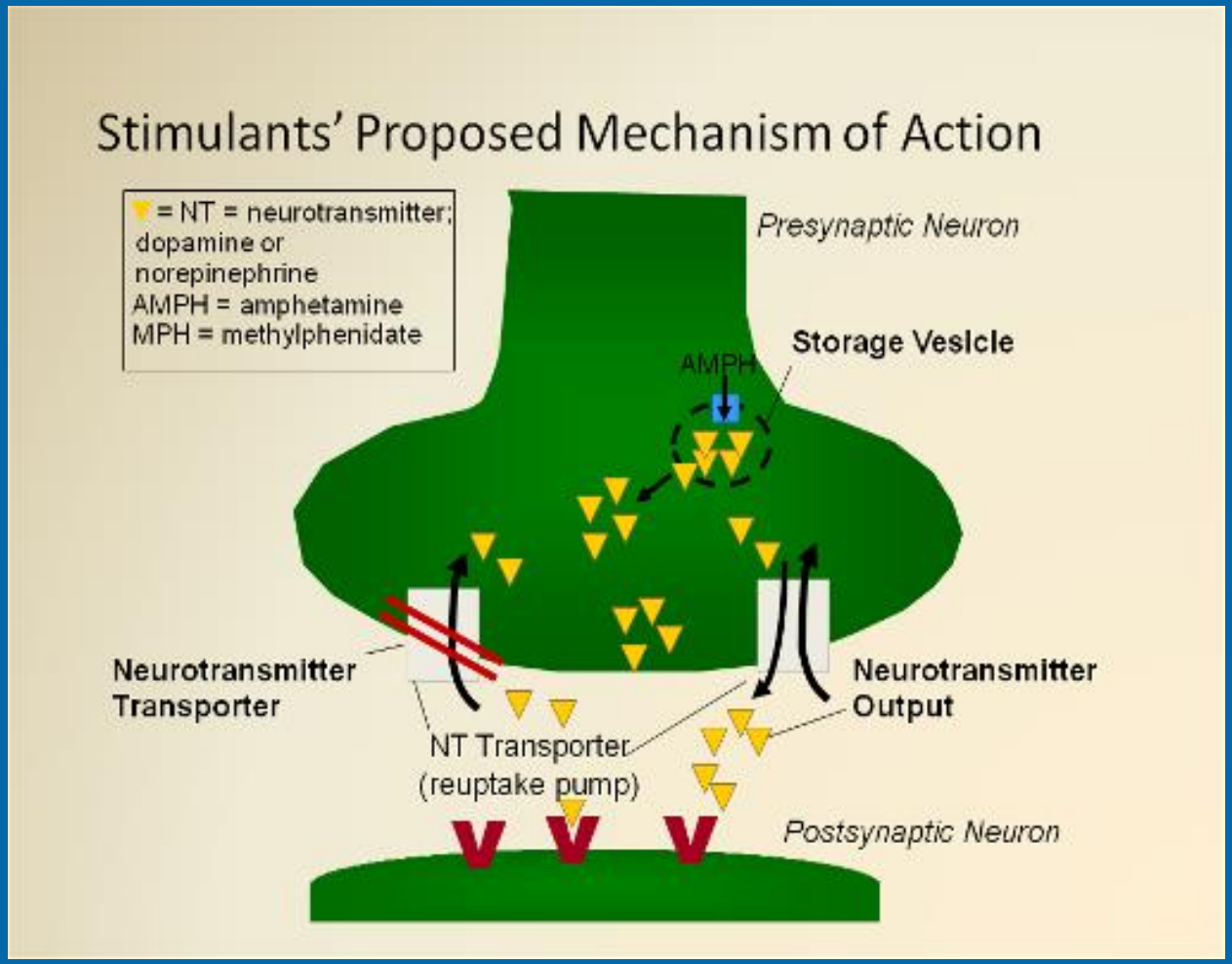
The MTA Cooperative Group, Arch Gen Psychiatry 1999;56:1073-1086.

Pharmacologic Management



Scientific American, September, p. 47

Stimulants' Proposed Mechanism of Action



First Line Pharmacologic Treatment

- Stimulants
  - Methylphenidate
  - Dexmethylphenidate
  - Mixed amphetamine
  - Dexroamphetamine
  - Lisdexamphetamine

- MPH and AMP equally effective.
- Similar adverse effects.
- Multiple current delivery systems.

Side Effects

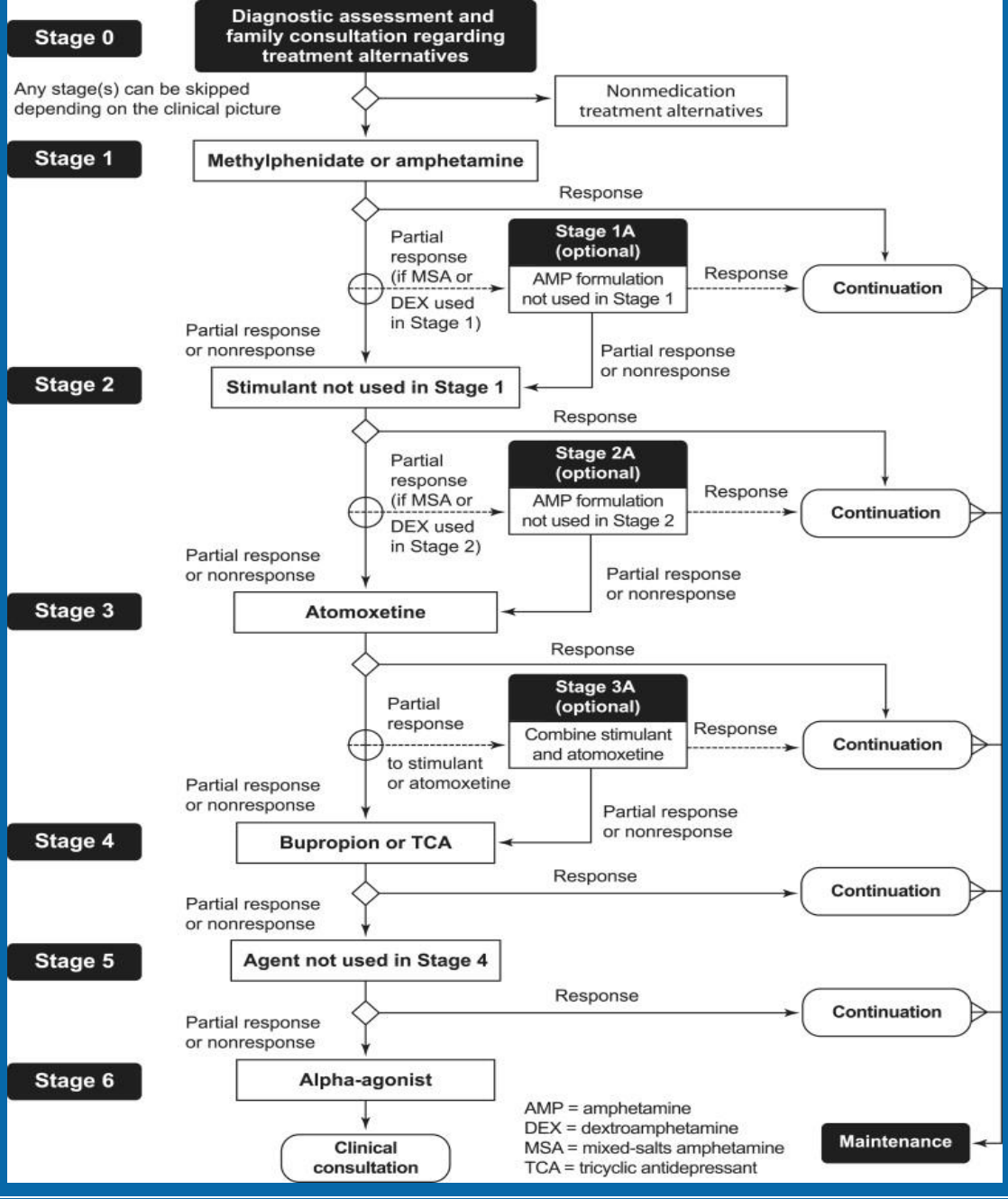
- Tachycardia
- Chest Pain
- Insomnia
- Growth Deceleration (?)
- Anorexia
- Dysphoria
- Tics
- Headaches
- Hypertension
- Anxiety

Contraindications

- HTN
- Hyperthyroidism
- Glaucoma
- Drug dependence
- Cardiac abnormality
- Concurrent use with MAO inhibitors
- Psychosis
- Anxiety
- Tics
- Seizure disorder not being treated

What if Stimulants Don’t Work

- Atomoxetine (Strattera)
- Buproprion (Wellbutrin)
- Modafinil (Provigil)
- Alpha-2 Agonist
  - Clonidine/Clonidine XR
  - Guanfacine/Guanfacine XR
- Tricyclic Antidepressants
  - Nortriptyline (Pamelor, Norpramin)
- Combination


Stage 0
Diagnostic assessment and family consultation regarding treatment alternatives
Any stage(s) can be skipped depending on the clinical picture
Nonmedication treatment alternatives
Stage 1
Methylphenidate or amphetamine
Response
Partial response (if MSA or DEX used in Stage 1)
Stage 1A (optional)
AMP formulation not used in Stage 1
Response
Continuation
Partial response or nonresponse
Partial response or nonresponse
Stage 2
Stimulant not used in Stage 1
Response
Partial response (if MSA or DEX used in Stage 2)
Stage 2A (optional)
AMP formulation not used in Stage 2
Response
Continuation
Partial response or nonresponse
Partial response or nonresponse
Stage 3
Atomoxetine
Response
Partial response to stimulant or atomoxetine
Stage 3A (optional)
Combine stimulant and atomoxetine
Response
Continuation
Partial response or nonresponse
Partial response or nonresponse
Stage 4
Bupropion or TCA
Response
Continuation
Partial response or nonresponse
Stage 5
Agent not used in Stage 4
Response
Continuation
Partial response or nonresponse
Stage 6
Alpha-agonist
Clinical consultation
AMP = amphetamine
DEX = dextroamphetamine
MSA = mixed-salts amphetamine
TCA = tricyclic antidepressant
Maintenance

Non-Pharmacologic Management

- Cognitive Behavioral Therapy
- Intensive behavioral programs
- School Interventions
- CAM interventions
  - Diet
  - Herbal
  - Vitamins
  - Biofeedback

Refractory ADHD

- 30 % of patients do not respond or cannot tolerate stimulants
- Comorbidities are the rule, not the exception
- Development is key when diagnosing psychiatric illness

The Treatment Refractory Decision Tree

- No response vs. side effects
  - No response
    - First review compliance
    - Consider genetic Variance
    - Question the diagnosis
    - Assess for comorbidities
    - Are non-pharmacologic interventions being maximized
  - Side effects
    - Weigh the side effect severity vs. the benefit
    - Work through the pharmacologic algorithm

Comorbidities

- Physical
  - Asthma
  - Eczema
  - Allergies
  - TIB
  - Epilepsy

- Mental
  - Oppositional Defiant Disorder = 54%-67%
  - Conduct Disorder = 26%
  - Mood Disorders = 20%-30%
  - Substance Abuse = 12%-24%
  - Anxiety Disorders = 10%-40%
  - Tic Disorders = 18 %

ADHD + ODD/Conduct

- Dependent on Severity of Comorbid Illness

- Stimulants or Atomoxetine
- Stimulants + Behavioral Therapy
- Stimulants + Behavioral Therapy + Alpha agonist
- Stimulants + Behavioral Therapy + SGA
- Legal Consequences + MST

(Hazell, P. Australasian Psych, 2010)

ADHD + Mood Disorders

- Treat mood disorder first
- ADHD + BD
  - SGA then add stimulant
  - Mood Stabilizer + Stimulant
  - Alternatively Atomoxetine, alpha agonist, or Buproprion
- Caution with BD for possible mood destabilization

- ADHD + MDD
  - Buproprion
  - SSRI + Stimulant
  - SSRI + CBT
  - Nortirptyline
  - Atomoxetine
  - SGA + Stimulant
  - Modafinil (motivation)

Bond, DJ. et al. CANMAT, 2012

ADHD + Substance Abuse

- Stabilization of Substance Abuse
- Controversy regarding effect of SA with use of stimulants
- Management Strategy
  - Atomoxetine or Buproprion
  - Stimulants (OROS methylphenidate or Lisdexamphetamine)
  - Alpha Agonists

ADHD + Anxiety

- Atomoxetine
- SSRI + stimulant or alpha agonist
- CBT + stimulant or alpha agonist
- TCA

ADHD + Tics

- Stimulant effects
  - May transiently exacerbate underlying Tic disorders
  - No longstanding differences in Tic course +/- stimulant use (Spencer, et al., Arch Gen Psych, 2001)
- Alpha Agonists
  - Effective for both disorders
- Atomoxetine
  - Does not exacerbate and may reduce tics

Combination Treatment

- Stimulant + Atomoxetine
  - Improvement of symptoms of hyperactivity and inattention as compared to either the stimulant or atomoxetine alone (Wilens, et al. J. Child Adolesc Psychopharm, 2009)
  - Increased Side effects include:
    - Appetite loss (14% to 40%)
    - Insomnia (14% to 52%)
    - Irritability (16% - 32%)
- Stimulant + Alpha Agonist
  - Improvement of symptoms of hyperactivity and inattention as compared to stimulant + placebo (Wilens, et al. J Am Acad Child Adolesc Psych 2012)
  - No change in side effects from either group

Novel Agents

- Memantine
- Nicotinic Receptor Agonist
- Melatonin

Summary

- ADHD can be differentiated from other disorders with a proper assessment
- Management can be undertaken in an algorithmic fashion
- Comorbidity is the rule and not the exception.