Overview

1. ADHD is a common neuro-development disorder.
2. ADHD predisposes individuals to TBI because of impulsive, hyperactive, inattentive behavior.
3. Patients with TBI can develop Secondary ADHD.
4. Patients with ADHD are poor drivers and are at higher risk for motor vehicle accidents and subsequent TBI.
5. ADHD and S-ADHD can be effectively treated.
Objectives

1. To understand the epidemiology of ADHD in children and adults.
2. To understand the connection between ADHD and brain injury and the development of secondary ADHD.
3. To be aware of the driving risks associated with ADHD.
4. To be able to treat ADHD and S-ADHD.
Overview of ADHD
ADHD – DSM-IV Definition

- Attention Deficit Hyperactivity Disorder (ADHD) is a neurobiological condition characterized by developmentally inappropriate levels of:
  - Inattention (concentration, distractibility)
  - Hyperactivity
  - Impulsivity

  in various combinations across school, work, home, and social settings.

- A disorder of “Executive Functioning”
- Symptoms leading to impairment before age 7
- Diagnosis for acquired problem after age 7 “ADHD NOS”
- No “adult” criteria in DSM-IV

Adapted from American Psychiatric Association, DSM-IV TR, 2000
Executive Functioning

1. Inhibition

2. Working Memory

3. Cognitive Flexibility
Changes to ADHD Criteria in DSM-5

1. Essentially the same symptom criteria as DSM-IV
   • 6 / 9 Inattention and hyperactivity/impulsivity

2. Language has been added for adult symptoms
   Example:
   1 (d) often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace
   • Adult diagnosis 5 / 9 from each category

3. Age of onset changed from 7 to 12

4. Can be co-morbid with Autism Spectrum Disorder
ADHD: Etiology

ADHD is a heterogeneous behavioral disorder with multiple possible etiologies.

- Neuroanatomic
- Neurochemical
- CNS insults
- Genetic origins
- Environmental factors

CNS; central nervous system.

## Pharmacological Treatments for ADHD September 2013 - CANADA

<table>
<thead>
<tr>
<th>Medications available and illustrations</th>
<th>Duration of action</th>
<th>Starting dose</th>
<th>Dose titration as per product monograph</th>
<th>Dose titration as per CADDRA <a href="http://www.caddra.ca">www.caddra.ca</a></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AMPHETAMINE-BASED PSYCHOSTIMULANTS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dextroamphetamine*</td>
<td>~ 4 h</td>
<td>tablets = 2.5 to 5 mg BID</td>
<td>↑ 2.5 - 5 mg at weekly intervals; max. dose/day: (q.d. or b.i.d.) All ages = 40 mg</td>
<td>↑ 2.5 - 5 mg/day at weekly intervals max. dose/day: (q.d. or b.i.d.) Children and Adolescents = 20 - 30 mg Adults = 50 mg</td>
</tr>
<tr>
<td>Dextroamphetamine*</td>
<td>~ 6 - 8 h</td>
<td>spansules = 10 mg q.d. a.m.</td>
<td></td>
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</tr>
<tr>
<td>Adderall XR*</td>
<td>~ 12 h</td>
<td>5 - 10 mg q.d. a.m.</td>
<td>↑ 5 - 10 mg at weekly intervals max. dose/day: Children = 30 mg Adolescents and Adults = 20-30 mg</td>
<td>Children: ↑ 5 mg at weekly intervals max. dose/day: Adolescents and Adults: ↑ 5 - 10 mg at weekly intervals max. dose/day: 50 mg</td>
</tr>
<tr>
<td>Capsules 5, 10, 15, 20, 25, 30 mg</td>
<td></td>
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<tr>
<td>Vyvanse*</td>
<td>~ 13 - 14 h</td>
<td>20 - 30 mg q.d. a.m.</td>
<td>↑ by clinical discretion at weekly intervals max. dose/day: All ages = 60 mg</td>
<td>↑ 10 mg at weekly intervals max. dose/day: Children = 60 mg Adolescents and Adults = 70 mg</td>
</tr>
<tr>
<td>Capsules 20, 30, 40, 50, 60 mg</td>
<td></td>
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<tr>
<td><strong>METHYLPHENIDATE-BASED PSYCHOSTIMULANTS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methylphenidate*</td>
<td>~ 3 - 4 h</td>
<td>5 mg b.i.d. to i.i.d. Adult = consider q.i.d.</td>
<td>↑ 5 - 10 mg at weekly intervals max. dose/day: All ages = 60 mg</td>
<td>↑ 5 - 10 mg at weekly intervals max. dose/day: Children and Adolescents = 60 mg Adults = 100 mg</td>
</tr>
<tr>
<td>(generic)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>10, 20 mg (Ritalin*)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biphetin*</td>
<td>~ 10 - 12 h</td>
<td>10 - 20 mg q.d. a.m.</td>
<td>↑ 10 mg at weekly intervals max. dose/day: Children and Adolescents = 60 mg Adults = 80 mg</td>
<td>↑ 10 mg at weekly intervals max. dose/day: Children = 60 mg Adolescents and Adults = 80 mg</td>
</tr>
<tr>
<td>Capsules 10, 15, 20, 30, 40, 50, 60, 80 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concerta*</td>
<td>~ 10 - 12 h</td>
<td>18 mg q.d. a.m.</td>
<td>↑ 18 mg at weekly intervals max. dose/day: Children = 54 mg Adolescents = 54 mg / Adults = 72 mg</td>
<td>↑ 18 mg at weekly intervals max. dose/day: Children = 72 mg Adolescents = 90 mg / Adults = 108 mg</td>
</tr>
<tr>
<td>Extended Release Tabs 18, 27, 36, 54 mg</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>NON PSYCHOSTIMULANT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strattera* (Atomoxetine)</td>
<td>Up to 24 h</td>
<td>Children and Adolescents: 0.5 mg/kg/day Adults = 40 mg q.d. for 7-14 days</td>
<td>Maintain dose for a minimum of 7 - 14 days before adjusting: Children = 0.8 then 1.2 mg/kg/day 70 kg or Adults = 60 then 80 mg/day max. dose/day: 1.4 mg/kg/day or 100 mg</td>
<td>Maintain dose for a minimum of 7 - 14 days before adjusting: Children = 0.8 then 1.2 mg/kg/day 70 kg or Adults = 60 then 80 mg/day max. dose/day: 1.4 mg/kg/day or 100 mg</td>
</tr>
<tr>
<td>Capsules 10, 18, 25, 40, 60, 80, 100 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intuniv XR™ (Guanfacine XR)</td>
<td>Up to 24 h</td>
<td>1 mg</td>
<td>Maintain dose for a minimum of 7 days before adjusting per 1 mg increment max. dose/day : Children 6-12 years = 4 mg</td>
<td>Maintain dose for a minimum of 7 days before adjusting per 1 mg increment max. dose/day : Children 6-12 years = 4 mg</td>
</tr>
<tr>
<td>Extended release tabs 1, 2, 3, 4 mg</td>
<td></td>
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</tr>
</tbody>
</table>

Illustrations do not reflect real size of pills/capsules.

Note: For specific details on how to start, adjust and switch ADHD medications, clinicians are invited to refer to the Canadian ADHD Practice Guidelines (www.caddra.ca)

This table was developed jointly by développement professionnel continu, Laval University, Quebec (www.fmed.ulaval.ca/fmc) and CADDRA (www.caddra.ca)
ADHD – A Very Impairing Condition

1. Education
2. Occupation
3. Driving and Accidents
4. Other Comorbidities
Long-term Educational Impairment

- Did not graduate college
- Drop-out
- Expulsion
- Suspension
- Grade retention

% of Sample

Change Jobs More Often

More Likely to Be Fired

Odds Ratio

Control

ADHD

Barkley RA. J Clin Psychiatry. 2002;63(suppl 12):10-15
CADDRA Canadian ADHD Practice Guidelines
Third Edition available to order or download at
www.caddra.ca
Traumatic Brain Injury
Definitions

- TBI is an insult to the brain caused by an external force that results in transient or permanent impairment
  - Cognition
  - Behavior
  - Emotional Functioning
  - Physical Functioning
Epidemiology

• TBI in the U.S. 1.4 – 3 million per year

• In 2003:
  • 1.2M Emergency visits
  • 290,000 hospitalizations
  • 51,000 deaths

• Substance abusers at higher risk

• 40 – 60% of TBIs are caused by motor vehicle accidents

• Cost of TBI $100 billion annually

Epidemiology

- Sex ratio M:F, 2:1
- Highest hospitalization rate
  1. 65+
  2. 15 – 44
  3. 45 – 65
  4. < 15
- Classification
  1. Mild – 50 - 90%
  2. Moderate 5 – 20%
  3. Severe 5 – 23%
Risk of Additional Brain Injuries

One Previous TBI  
risk  2.8 – 3.0

Two Previous TBIs  
risk  7.8 – 9.3

Cause: Continued exposure to risk factors  
eg. Sports, alcohol

Primary Injury

• Temporal and frontal lobes most susceptible (neurobehavioral syndromes) because of the spatial arrangement of the brain

• Some animals cannot be usually concussed because of brain architecture – e.g. the woodpecker
Secondary Injury

- Brain injury due to other associated problems
  - Hypoxia
  - Intracranial pressure (neurosurgical emergency)
  - Pyrexia/infection
  - A thorough review of medical records is essential
CT and MRI are not very sensitive in detecting Diffuse Axonal Injury (DAI).

DAI is disruption of individual nerve cells.

MRI techniques:

1. T2 weighted, gradient recalled echo (GRE)
2. Susceptibility weighted imaging (SW1)
3. A bigger magnet gives better imaging - 3T better than 1.5
4. Magnetic resonance spectroscopy (MRS)
5. Diffusion Tensor Imaging (DTI)

Ashwal, S. SWI and MRS in Assessment of Outcome After Pediatric TBI
Arch Phys Med Rehab 87 Dec 2006 S50 - 58
The White Matter

From: The Virtual Hospital (www.vh.org); TH Williams, N Gluhbegovic, JY Jew
White Matter Damage Is Common

Pediatric Neurology
Volume 30, Issue 2,
February 2004, Pages 140-142
## Categorization of TBI

<table>
<thead>
<tr>
<th>Minor (GCS 15)</th>
<th>Mild (GCS 13)</th>
<th>Moderate (GCS 12)</th>
<th>Severe (GCS 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concussion (1) Grade 1</td>
<td>Grade 2</td>
<td>Grade 3</td>
<td></td>
</tr>
<tr>
<td>LOC 0</td>
<td>&lt; 1 min</td>
<td>&lt; 30 min</td>
<td>30 min - 1 week</td>
</tr>
<tr>
<td>PTA &lt; 30 min</td>
<td>&gt; 30 min - 24 hr</td>
<td>&lt; 24 hours</td>
<td>24 hrs – 1 week</td>
</tr>
<tr>
<td>Type of Injury</td>
<td>Reversible physiological abnormalities</td>
<td>DAI</td>
<td>Possible → Probable structural lesions</td>
</tr>
</tbody>
</table>

Note: Data Driven Revised Cantu Criteria, Cantu J, Journal of Athletic Training 2001

Also see page 626 DMS-5

(1) *Data Driven Revised Cantu Criteria, Cantu J, Journal of Athletic Training 2001*
A major advance!

Table 1 (page 593) lists 6 domains of cognitive functioning.

1. Complex attention
2. Executive functioning
3. Learning and memory
4. Language
5. Perceptual – motor
6. Social cognition
Neurocognitive Disorders

Major and Mild Neurocognitive Disorders

A. Decline in cognitive functioning

B. Interference with ADL’s

• 13 subsets including Alzheimer’s and Traumatic Brain Injury
Major or Mild Neurocognitive Disorder Due to Traumatic Brain Injury

A. The criteria are met for major or mild neurocognitive disorder

B. There is evidence of a traumatic brain injury—that is, an impact to the head or other mechanisms of rapid movement or displacement of the brain within the skull, with one or more of the following:
   - Loss of consciousness
   - Posttraumatic amnesia
   - Disorientation and confusion
   - Neurological signs (e.g. Neuroimaging demonstrating injury; a new onset of seizures; a marked worsening of a pre-existing seizure disorder; visual field cuts; anosmia; hemiparesis)

C. The neurocognitive disorder presents immediately after the occurrence of the traumatic brain injury or immediately after recovery of consciousness and persists past the acute post-injury period
1. Attention – Secondary ADHD (S-ADHD)  
   – sustained and divided is more affected than focused attention
2. Memory
   – worst - encoding, storing, retrieving new information
3. Executive functioning
   – associated with frontal lobe damage
4. Intellectual functioning
   – correlates with severity
   – performance IQ more commonly affected than verbal
5. Language
   – articulation
   – expressive language
   – language comprehension

6. Visual perception
   – diplopia
Problems of Executive Functioning

1. Poor planning
2. Poor problem solving
3. Reduced capacity for abstract thought
4. Slowed speed of response
5. Poor response inhibition

The principle cause of impaired activities of daily living (ADLs) is cognitive disturbance associated with executive dysfunction.

Anderson V (2001) Developmental Neuropsychology
Types of Attentional Problems

- Selective
- Sustained
- Divided
- Response inhibition
Secondary - ADHD

1. Term first used by Gerring to describe acquired ADHD post brain injury
2. 99 children with moderate or severe traumatic brain injury
3. Premorbid ADHD – 20%
4. An additional 19% developed ADHD
5. These children had “high psychosocial adversity”

Pediatric Traumatic Brain Injury and Secondary ADHD

<table>
<thead>
<tr>
<th>Study (year)</th>
<th>Subjects (n)</th>
<th>Age (years)</th>
<th>Mean age of injury (years)</th>
<th>Years post-TBI</th>
<th>Diagnostic criteria</th>
<th>SADHD rate (%)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gerring et al. (1998)</td>
<td>99</td>
<td>4–19</td>
<td>10.69</td>
<td>All assessed at 1 year post-TBI</td>
<td>DSM-III-R</td>
<td>19</td>
<td>[17]</td>
</tr>
<tr>
<td>Konrad et al. (2000)</td>
<td>27</td>
<td>4–11</td>
<td>9.1</td>
<td>6 months–6 years</td>
<td>DSM-IV</td>
<td>48</td>
<td>[73]</td>
</tr>
<tr>
<td>Bloom et al. (2001)</td>
<td>36</td>
<td>6–15</td>
<td>9.3</td>
<td>All assessed at least 1 year post-TBI; range: NA</td>
<td>DSM-IV</td>
<td>44</td>
<td>[74]</td>
</tr>
<tr>
<td>Schachar et al. (2004)</td>
<td>137</td>
<td>5–17</td>
<td>Not reported</td>
<td>All assessed at least 2 years post-TBI; range: NA</td>
<td>DSM-based research criteria</td>
<td>35</td>
<td>[75]</td>
</tr>
<tr>
<td>Yeates et al. (2005)</td>
<td>41</td>
<td>6–12</td>
<td>9.7</td>
<td>4; range: 2.37–5.84 years</td>
<td>DSM-IV</td>
<td>20</td>
<td>[14]</td>
</tr>
<tr>
<td>Levin et al. (2007)</td>
<td>114</td>
<td>5–15</td>
<td>10</td>
<td>All assessed at 2 years post-TBI</td>
<td>DSM-IV</td>
<td>19</td>
<td>[10]</td>
</tr>
</tbody>
</table>

DSM: Diagnostic and Statistical Manual of Mental Disorders; DSM-III-R: Diagnostic and Statistical Manual of Mental Disorders third edition, Revised; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders fourth edition; NA: Not available; SADHD: Secondary ADHD; TBI: Traumatic brain injury.
Neurocognitive Deficits with Pre-existing ADHD

• Compared with TBI only, patients with TBI and pre-existing ADHD had worse performance on measures of attention, executive functioning and memory.
Treatment of TBI
TREATMENT

1. Standard diagnoses require standard evidence-based treatment

   e.g. Mood Disorder
   - Cognitive / behavioral psychotherapy
   - ± SSRI medication

2. Learning / academic problems
   - Specialized education

3. Address diagnoses of pain and sleep
4. Problems with attention, short-term memory, information processing
   a) Trials of stimulant medication
      (treat as ADHD)
   b) ? Cholinergic augmentation
      - Donepezil
   c) Cognitive retraining
      - Use a manualized approach

1 Whyte J. et. al, Psychostimulant use in TBI rehab, J. Head Trauma 2002: 17 284-99
3 Yoo JH 2007, J. Autism Dev. Disorders 37: 1883-1901
5 Galbiati S et. al., 2009 Neuropsych 23: 40-49
TREATMENT

5. Individual and Family Therapy
6. Bibliotherapy \(^1\)
7. Part of the rehab team \(^2\)


\(^2\) Sherwin E. Et. al., The trauma of pediatric and adolescent brain injury: issues and Implications for rehab specialists *Brain Injury* 2000, 267 -284
Pharmacological Treatment of Neurobehavioural Sequelae of TBI

Outcomes

1. Psychiatric Disorders
   a) Depression – 25 – 60% develop depression within 8 years
   b) Anxiety – risk factor of 2 – 6 times

2. Cognitive deficits – problems with
   a. Attention – processing speed
   b. Memory
   c. Executive functioning

3. Aggression - 35 – 96% in acute phase

Recommendations organized as:

1. Standards
2. Guidelines
3. Options

Warden, D., Guidelines for the Pharmacologic Treatment of Neurobehavioral Sequelae of Traumatic Brain Injury J of Neurotrauma, 2006
Nov. 1468 - 1501
Other Treatment - Amantadine

Amantadine

- Used in Parkinson’s Disease
- Mechanism unknown but probably releases dopamine
- Target Symptoms
  1. Arousal
  2. Agitation
  3. Executive functioning
- 5 papers, less than 100 subjects
- No double blind, randomized studies

“Amantadine is clinically beneficial for children who have sustained head injuries particularly for symptoms of alertness and arousal”

William, S.  Amantadine Treatment Following TBI in Children Brain Injury August 2007, 885 - 889
Psychostimulants in Traumatic Brain Injury

Target Symptoms

1. Inattention
2. Distractibility
3. Disorganization
4. Hyperactivity
5. Disinhibition
6. Impulsiveness
7. Emotional lability

Evans, R.W., Treatment of Chronic Closed Head Injuries with Psychostimulants. J. Nerv. Mental Disorders 175, 106, 1987
Noradrenergic Agonists for Acute Traumatic Brain Injury

- The gold standard – *The Cochrane Database of Systematic Reviews*

- Amphetamines (and other noradrenergic agonists) may have potential after brain trauma including TBI and strokes but there are no good controlled trials

Psychostimulants in TBI and Attention

Review Article

- “It is likely that methylphenidate and dextroamphetamine improve some but not all aspects of attention” following TBI.

Measures of Attention

1. Vigilance/sustained attention
2. Processing speed
3. Distractibility

Cognitive Dysfunction Post TBI
A Dopamine Hypothesis

- Good review that makes sense out of why.
  1. Methylphenidate
  2. Amantadine
  3. Bromocriptine
- All can enhance cognitive functioning by enhancing dopamine.

ADHD and Driving

? A Public Safety Issue
Key Messages

1. ADHD is a common impairing condition arising in childhood and persisting into adulthood.

2. The symptoms of ADHD, inattention, hyperactivity and impulsivity result in poor driving skills and increased accident rates.

3. One of the risks of MVA’s is traumatic brain injury and specifically damage to the frontal lobes of the brain resulting in acquired or secondary ADHD.

4. Both ADHD and S-ADHD are disorders of executive functioning.
Nicolas Cugnot who designed the first car in 1769 made another steam-driven vehicle two years later, also at the Paris Arsenal. The machine reportedly ran quite well, although on one occasion it ran into a wall, thus recording the world's first motor-accident. The vehicle may still be seen today in the Conservatoire Nationale des Arts et Metiers in Paris.

Currently 1.2 million people die in MVC and 50 million are injured worldwide (WHO 2002)
Motor Vehicle Accidents

1. WHO 1.2 million deaths annually
   50 million - injured

2. In high income countries – leading cause of death ages 4 – 29


   • “Road Safety is No Accident”
   • Aimed to reduce MVA by 30% by 2010
ADHD and Driving: A Dangerous Mix

- Motor vehicle accidents are the leading cause of death in adolescents, and ADHD is a major contributor.¹

- Young drivers with ADHD are
  - 2 to 4 times more likely to have traffic accidents.²-⁴
  - 3 times as likely to have injuries.³
  - 4 times as likely to be at fault.²
  - 6 to 8 times more likely to have their license suspended.²,³

- This extends to females as well as males.⁵

Motor Vehicle Accidents
“Preventable Co-morbidity”

“Stimulants most likely reduce the risk of moving violations and crashes for drivers with ADHD”

“Long-acting stimulants will likely reduce driving risk”
1. Take prescribed stimulant medication before driving. The medication must be in the body at the time of driving for it to have an effect. Avoid driving during the rebound time, when the medication has just left the system and ADHD symptoms are correspondingly on the increase.

2. Manual transmission! Research on ADHD and driving shows that a manual transmission helps as it increases the arousal and attention levels, and may also increase awareness of speed.

3. Recognize that driving and ADHD is a danger. There is a much greater risk of accidents for people with ADHD, mostly due to speed, on top of the greater risk for teen drivers in general.

4. Consider limiting your driving to times when you are fresh – e.g. not at night.
Tips For ADHD & Driving

5. Keep all phone off and in the glove compartment.

6. Choose one radio station and do not change it while driving, or use on CD.

7. No passengers.

8. Avoid rush hours.

9. Allow plenty of time, extra time so as not to be in a rush.

10. Plan trips ahead of time to reduce the distraction of looking for directions or looking at the map.

11. Acquire ample driving practice (consider extra lessons).

12. No food while driving.

13. Read road signs and speed limits out loud to yourself.
Other Studies

- ADHD drivers \(^1\)
  1. Drive more kilo meters / year
  2. More citations, more fines
  3. More MVAs
  4. Self described driving – more insecure & hectic

- ADHD drivers become fatigued more quickly than controls. \(^2\)

- Review Article - well documented driving risks associated with ADHD and positive effects of stimulant medication and is the only treatment that improves driving. \(^3\)

ADHD & Alcohol

- 15 adults ADHD, 23 controls
- Measures – driving simulator
- Sober ADHD drivers resembled intoxicated drivers at the level of blood alcohol defining impairment.
- Intoxicated ADHD drivers were worse than intoxicated normal controls, \(^1,^2\)

1. Weafer JW, 2008 *Exp Clin Psycho Pharm*; 16(3) 251-263
2. Barkley RA, 2006 *Neuropsych*; 20:77-87
Take-Home Messages

1. Talk to your ADHD patients about increased risk, costs, and legal implications of driving mishaps
2. Assure patients (and parents) of the beneficial effects of medication and the need to take it daily
3. Only drive when medication is effective
Summary

1. ADHD results in poor driving skills and increased MVAs and TBIs.
2. Damage to the frontal lobes can produce S-ADHD.
3. Both ADHD and S-ADHD can be treated effectively with stimulants to reduce impairing symptoms and improve driving behaviors.
TBI References

6. Management of Adults with Traumatic Brain Injury (2013), David Arciniegas