ADHD

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Overview

- Case Example.
- Epidemiology.
- Diagnostic Criteria.
- ADHD across the Lifespan.
- Aetiology.
- Treatment.
- Prognosis.

ADHD - Epidemiology

- Prevalence of ADHD in children: 5.3% (6.5% for children, 2.7% for adolescents).
- ***Polanczyk G. et al. The worldwide prevalence of ADHD: a systematic review and metaregression analysis Am J Psych.(2007) 164 942-948.***
- Prevalence of ADHD in adults: 2.5% (95% C.I. 2.1-3.1). Six studies, large community samples.
- ***Simon V et al. Prevalence and correlates of adult attention-deficit hyperactivity disorder: meta-analysis. BJP (2009) 194 204-211.***

ADHD

Core Symptoms:

- Hyperactivity: a restless and shifting excess of movement
- Impulsivity: premature, thoughtless actions.
- Inattention: a disorganised style preventing sustained effort.
- M:F 4:1 ; No definitive biological or psychological test for ADHD.

Information Processing

- Sustained Attention: midbrain (reticular formation and thalamic nuclei) and brainstem; shows significant development from the age of 11 to adulthood.
- Selective Attention: temporal and parietal cortex and corpus striatum; matures to adult level before the age of 7.

Information Processing

- Shifting Attention: prefrontal cortex, medial frontal lobe, anterior cingulate gyrus; develops rapidly between the ages of 7 and 9.
- Speed of Processing: increases through childhood to early adulthood.

Executive Function

- Control of attention.
- Strategic planning.
- Problem-solving.

- Prefrontal cortex

DSM-IV – ADHD - Inattention

- Often fails to give close attention to detail or makes careless mistakes in schoolwork, work or other daily activities.
- Often has difficulty sustaining attention on tasks or play activities.
- Often does not follow through on instructions and fails to finish schoolwork, chores or workplace duties.

DSM - ADHD - Inattention

- Often has difficulty organising tasks and activities.
- Often avoids, dislikes or is reluctant to do tasks requiring sustained effort.
- Often loses things.
- Is often easily distracted.
- Is often forgetful in daily activities.

DSM IV – ADHD - Hyperactivity/Impulsivity

Hyperactivity:

- Often fidgets with hands or feet or squirms in seat.
- Often leaves seat in classroom or other situation where remaining seated is expected.
- Often runs or climbs excessively where inappropriate (feelings of restlessness in youth or adults).

DSM – ADHD – Hyperactivity/Impulsivity

Hyperactivity:

- Often has difficulty playing quietly.
- Is often 'on the go' or often acts as if 'driven by a motor'.
- Often talks excessively.

DSM IV – ADHD – Hyperactivity/Impulsivity

Impulsivity:

- Often blurts out answers.
- Often has difficulty waiting their turn.
- Often interrupts or intrudes on others.

DSM IV - ADHD

- Symptoms present before the age of 7.
- Impairment in two or more settings.
- Significant impairment in social, school or work functioning.

DSM IV - ADHD

Subtypes:

- Combined type.
- Predominantly inattentive type.
- Predominantly hyperactive-impulsive type.

Validity of the Diagnosis

- A. To what extent do the phenomena of hyperactivity, impulsivity and inattention cluster together in the general population and into a particular disorder that can be distinguished from other disorders and from normal variation?
- B. Is the cluster of symptoms that defines ADHD associated with significant clinical and psychosocial impairment?

Validity of the Diagnosis

- C. Is there evidence for a characteristic pattern of developmental changes, or outcomes associated with the symptoms that defines ADHD?
- D. Is there consistent evidence of genetic, environmental or neurobiological risk factors associated with ADHD?

ADHD Across the Lifespan

- The problems associated with ADHD differ across the lifespan as the brain matures and the need for sustained self-control increases.
- Preschool: excessive, incessant, demanding activity; School-age: core symptoms; Adolescent: fidgety and inattentive; Adult: inner restlessness, poor work performance, increased accidents.

ADHD in Adults

- Symptomatic > syndromatic.
- Similar numbers of males and females.
- Inattention > hyperactivity/impulsivity.
- Familiality stronger in adults with ADHD than children with ADHD (57% vs. 15%)

ADHD - Aetiology

- ADHD is a complex polygenetic disorder wit high levels of heterogeneity influenced by the interaction of multiple aetiological factors.
- Genetic.
- Environment.

Genetics

- ADHD aggregates in families with a 3-5 times increased risk in first degree relatives.
- Several genes of small effect.
- Behavioural genetic studies suggest a heritability of 0.6 – 0.9.

ADHD - Genetics

- Genes potentially involved in ADHD for which there are replicated findings:
- Dopamine receptor 4 (DRD4 7 repeat allele)
- Dopamine receptor 5 (DRD5 148 bp-allele)
- Dopamine transporter (DAT1 10 repeat-allele)
- Dopamine receptor gene (DRD1) and Serotonin receptor gene 5-HT (1B)
- Dopamine beta hydroxylase gene (Taq 1 polymorphism)
- SNAP-25 gene replicated findings

Genes and Response to Treatment

- Growing evidence that genes moderate treatment response in ADHD. For example:
- Total ADHD symptom control predicted by polymorphisms at COMT and the serotonin transporter (SLC6A3) intron 2 VNTR.
- The presence of the short allele of the serotonin transporter gene (s/s) increased the risk of depression in children with ADHD who were also exposed to maternal depression.

Environment

Potentially important environmental factors:

•Prenatal / perinatal complications, Low birth weight, Prenatal exposure to alcohol, benzodiazepines, nicotine, Brain diseases and injuries, severe early deprivation, institutional rearing, lead toxicity.

ADHD - Neurochemistry

- Dopaminergic hypoactivation of prefrontal and parietal cortex, caudate nucleus and cerebellum.
- Delayed cortical thickening in pre-frontal and occipital cortex and cerebellum.
- Prefrontal cortex involved in regulation of behaviour.
- Cerebellum and caudate nucleus involved in learning about the frequency and timing of events.
- Parietal cortex: connects to prefrontal cortex to bias attention in one area or another.

Common Problems associated with ADHD in Children

- Non-compliant behaviour. Aggression. Tantrums. Unpopular with peers.
- Sleep disturbance.
- Specific learning disorders.
- Tics.
- Mood changes e.g. irritability.
- Clumsiness.
- Immature language.

Differential Diagnoses

- Mental retardation/ Specific learning disorders. Autistic spectrum disorders.
- ODD/CD.
- Anxiety and mood disorders.
- Attachment disorders.
- Tic disorders.

BUT: all can occur co-morbidly with ADHD.

Exclude hearing impairment, epilepsy.

Management

- Biological: Medication (from school age)
- Psychological: Psycho-education for parents and school, behaviour management training, parental support.
- Social: Child Disability Allowance, Needs Assessment.

Stimulant Medication

- Methylphenidate, dexamphetamine.
- Inhibitor of dopamine transporter.
- Controlled drugs.
- Side-effects: appetite suppression, irritability, interference with sleep. Tics can emerge or worsen. Stimulants increase heart rate and blood pressure in a dose dependent but not clinically significant way.

Stimulant Medication - Growth

- Monitor height and weight 3-6 monthly. Initial weight loss over the first 2 months. After 3 years stimulant-treated children were 1-2.5 cm shorter than expected (not clinically significant). But some children have an idiosyncratic response.

Stimulant Medication - Sleep

- Stimulant-treated children have increased sleep latency (65 minutes compared to 26 minutes in non-treated), reduced total sleep (7.2 hours compared to 8.2 hours) but no difference in waking time or sleep efficiency.

Stimulants and the CVS

In 2005 the FDA gave a Black Box warning based on a review of 25 deaths (12 children) and 54 serious cardiac complications in patients taking stimulants in the USA between 1999 and 2003. This equated to < 2 non-fatal CVS events and < 1 death per million prescriptions, which is unlikely to be greater than the non-treated population.

Dosing of Stimulants

- Methylphenidate: Maximum dose: 60mg per day (as 20mg tds).
- Effective ½ hour after ingested. Duration of action of short-acting tablet: 4-6 hours.
- Increased release of catecholamines in the brain.
- Long-acting preparations: Concerta, Ritalin LA. Once-daily dose.

Advantages of Long-Acting Preparations

- Convenience. Compliance.
- Reduce stigma. Reduced potential for abuse or diversion.
- Pharmacological profile.

Immediate release preparations are used for initial titration.

Slower titration if co-morbid tics or epilepsy

Children who cannot have Stimulants

- Congenital heart defects.
- Severe tic disorders.
- Severe growth suppression.

Non-Stimulant Medication

- Atomoxetine (Strattera).
- Selective Noradrenaline Transporter Blocker.
- Once daily dosage. Full clinical effectiveness seen at 6-8 weeks.
- Side-effects: nausea, sedation, loss of appetite, increase in pulse and blood pressure. Uncommonly raised liver enzymes and urticaria.

Other Medication

- Clonidine and guanfacine – selective alpha-2 agonists.
- Strengthen working memory by inhibiting cAMP-HCN channel signalling in prefrontal cortex.
- Side-effects: sedation, headaches.
- Off-label use: e.g. risperidone, SSRIs.

Effectiveness

- Methylphenidate and atomoxetine are the only drugs with clear RCT evidence for effectiveness in treating ADHD with methylphenidate having the largest effect.
- "In school-age children with severe ADHD, drug treatment should be offered as a first-line treatment. Parents should also be offered a group-based parent-training education programme". (NICE, 2009)

Drug Interactions:

- Fluoxetine and paroxetine increase levels of stimulant medication.

Dietary Interventions

- "The elimination of artificial colouring and additives from the diet is not recommended as a generally applicable treatment for children and young people with ADHD".

NICE Recommendations (2009).

Multimodal Treatment Study of Children with ADHD (MTA)

Original study: n=579 children with ADHD. 6 sites.
Aged 7 – 9.9 years (1999).

Randomised to one of 4 groups for 14 months of treatment:

1. Medication plus monthly clinic review,
2. Behavioural intervention (27 sessions group parental training, 8 individual parent sessions, 8 week summer treatment programme, 12 weeks classroom-administered therapy, half-time teacher aide and 10 teacher-consultation sessions),
3. Medication plus Behavioural Intervention (Combined),
4. Usual Community Care.

MTA Study

- Initial findings: compared the 3 treatment groups with one another and with community care after 14 months of treatment. All groups showed some improvement.
- Combined Treatment and Medication management showed significantly greater improvements in ADHD and ODD than Behavioural Intervention or Community Care.
- Combination Treatment had significantly better outcomes for internalising symptoms, teacher-related social skills, parent-child relations and reading attainment than the other groups.

MTA Study

Three subgroups of ADHD trajectories were identified:

1. Class 1 (34%) showed a gradual improvement with increased significant benefit from medication at 3 years.

2. Class 2 (52%) large initial improvement that was maintained; tended to be of higher SES and lower behaviour problems at onset and were more likely to have received Combination treatment or medication treatment.

3. Class 3 (14%) initial improvement but return to pre-treatment symptoms.

MTA - Overall Findings

- Early ADHD symptom trajectory is most prognostic.
- Children with combined ADHD continue to have significant impairment in adolescence.

ADHD – Outcomes – Increased Risk of:

- Psychiatric co-morbidity: ODD/CD, anxiety and mood disorders, substance abuse/dependence.
- School: expulsion, poor academic grades.
- Accidents e.g. MVA.
- Unemployment.
- Family dysfunction and divorce.
- Social/legal/criminal problems.

DSM V

Considerations for ADHD and the Disruptive Behaviour Disorders:

ADHD: An older age-of-onset criterion.

1. Trying to establish valid diagnostic cut-offs across the lifespan.
2. How to handle the hierarchical exclusion of ADHD with ASD.
3. Considering alternatives to inattentive vs. hyperactive-impulsive symptom domains.

Conduct Disorder: Adding 'callous-unemotional traits' specifier.

Take-Home Messages

- ADHD is a common condition, persisting into adulthood in many cases, associated with significant impairment.
- Stimulant Medication is most effective. Short duration of action (<12 hours) gives great flexibility in management.
- Behavioural treatments needed for co-morbid oppositional defiant/conduct disorder symptoms.

Thank you

- Useful websites:
- http://www.nice.org.uk/CG72 (NICE ADHD Guidelines)
- http://www.psyq.nl/files/1263005/DIVA_2_EN.pdf (The Diagnostic Interview for ADHD in Adults (DIVA).
- www.caddra.ca (The Canadian Attention Deficit Hyperactivity Disorder Resource Alliance).