ADHD in children with neurological disorders

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Outline

- ADHD is a disorder of brain function
- How neurological disorders impair attention
- Which neurological disorders are associated with ADHD?
- What information do we have about treatment?

The neurological basis of attention

- **Abnormalities of brain structure have been reported in ADHD**
  - Total brain volume 5% smaller, cerebellar volumes smaller, caudate volumes smaller
  - Castellanos *et al* JAMA 288: 1740-1748
  - Frontal lobe, basal ganglia, cerebellum
  - Findings inconsistent
- **Functional studies**
  - Abnormal function of the fronto-cortical-striatal-thalamic circuitry
  - Activation of other areas not seen in controls
  - Roth R, Saykin A. Psych Clinics of North America, 27 1 2004, Durston S, Men Ret & Dev Dis Res Rev 9:184-95 2005.

Major components of frontal-striatal-thalamic cortical circuitry and other regions implicated in ADHD

Perhaps a regulator of the function of different regions of the cortex (controlling which regions are active).

Roth R, Saykin A. Psych Clinics of North America, 27 1 2004

Neurological disorders that impair attention

- **Damage to the neural pathways supporting attention**
  - Traumatic Brain Injury (~20%)
  - Stroke
  - Encephalitis
  - Spina-bifida with hydrocephalus (~30%)
- **Functional impairment of attention networks**
  - **Epilepsy**
  - ? Tourette syndrome (>50% ADHD clinical groups)

Stroke and ADHD

- **Children with stroke have a significantly increased risk of ADHD**
  - 15/25 stroke vs 6/25 control (p=0.03)
- **Lesion volume not associated with ADHD traits**
- **Small lesions of the putamen associated with ADHD**
  - ADHD 6/7 with putamen lesion versus 2/6 with no putamen lesion **(p=0.1)**
  - Max *et al J* Am Acad Ch Adol Psych 41 563-571 2002

Traumatic brain injury (TBI)

- **Incidence of ADHD after TBI (143 children)**
  - **15%** between 6-12 months after injury
  - **21%** more than 1 year after injury
- **Factors significantly predictive of ADHD**
  - Pre-injury adaptive function (Vineland)
  - Pre-injury psycho-social adversity
- **Factors not associated**
  - Size or site of lesion
  - Acute severity of neurological insult
  - Max *et al* J Am Acad Child Adol Pscych 44:1041-1049 2005
- **Methyl-phenidate is probably effective in treating ADHD in children with TBI**

Epilepsy

- **What is an epileptic seizure?**
  - A temporary involuntary impairment in brain function
  - Synchronised repetitive of nerve cells
  - There are many different types of seizures
    - Generalised Tonic Clonic – *"Grand mal"*
    - Partial (focal) seizures,
    - Absence
    - Complex partial
- **For a significant minority of children with epilepsy the cognitive effects are the most severe part of epilepsy**

How common are attention disorders in childhood epilepsy?

- **Attention disorders in childhood epilepsy:**
  - **ADHD in 4%** of children with epilepsy (epidemiological)
    - 67/10,316 children had epilepsy (~ 6 per 1000)
    - Davies S *et al*, Dev Med Ch Neurol 2003
  - **ADHD in 37.7%** of children with epilepsy of more than 6 months duration
    - 175 outpatient children/ used Child Behaviour Checklist
    - Dunn *et al* Dev Med Ch Neurol 45: 50-54 2003
  - **ADHD in 70%** of children with severe epilepsy
    - Children undergoing neuropsychological assessment for severe epilepsy (73% pre or post epilepsy surgery)
    - Sherman *et al Epilepsia 48(6) 1083-91, 2007.*

Is ADHD different in epilepsy?

- **ADHD is divided into three sub-types on DSM IV criteria**
  - Inattentive/ Hyperactive-Impulsive/ Combined (both of the above) – most common.
- **Inattentive sub-type most common in childhood epilepsy**
  - Dunn *et al* 175 children with epilepsy
  - **24%** Inattentive sub-type/ **11%** combined/ **2%** hyperactive
  - Sherman *et al* 203 children with severe epilepsy, heterogeneous sample (pre and **post** surgery for epilepsy)
  - **40%** had clinically significant impairments in inattention, **18%** hyper-activity impulsivity
- **Children may be less readily identified as having an attention disorder**

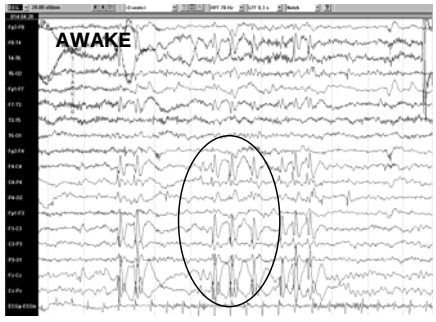
What causes ADHD in childhood epilepsy?

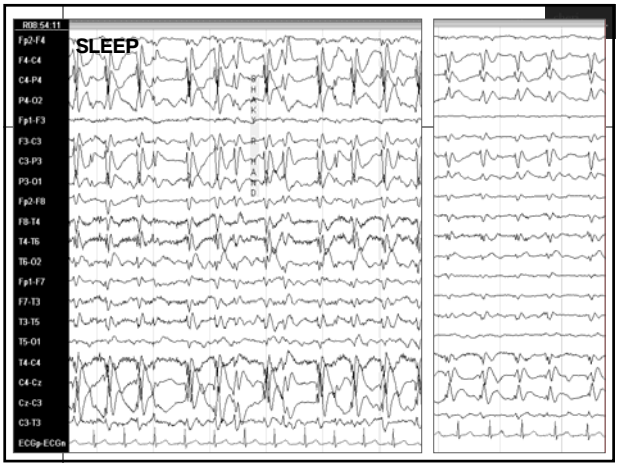
- **More severe epilepsy**
  - ↑ ADHD described in more severely affected groups
  - TLE – frequency of seizures associated with poor attention
- **Medications**
  - Probably **phenobarbitone**, **benzodiazepines**
  - **Topiramate –** obese children significantly elevated attention problems 3 months after starting treatment
  - Dose related, improved on lower doses
  - Aarsen FK *et al* Neurology 67: 1307-08 2006
- **Unclear whether medication causes these problems in children with improved seizure control**

… or something else?

- **Attention problems before seizures?**
  - 224 children first seizure/135 siblings
  - CBCL within 6 weeks of 1st seizure
  - 11% of children with epilepsy/ 3% siblings had attention problems 6 months (p=0.0001)
  - An unrecognized seizure ↑incidence of attention problems (15.8% vs 8.1%)
  - Austin *et al* Pediatrics 107,1,2001

Are impairments in attention related to epileptic discharges?





Attention disorders and epilepsy: A common cause?

- Biological factors that lead to epilepsy may impair the function of neurological systems required for attention
  - Eg Ion channel disorders

Are medications safe and effective in epilepsy + ADHD?

- **Methylphenidate is probably effective in children with epilepsy**
  - Two studies have found evidence of effectiveness
    - CPT improved in 70% (Gross-Tsur *et al* J Paeds 130 670-4 1997)
    - Conners' rating scale showed significant improvement (Gucuyener et al J Ch Neurol 2003 109-12)
- **Neither study showed evidence of increased seizures frequency**

Epilepsy or inattention?

	Epilepsy	Day-dreaming
Response to stimulus	No (usually)	Yes
Stereotyped	Yes	No
Associated movements	Yes (sometimes)	No
Timing	Interrupts conversation	Maths

Resected right and left hemispheric cerebellar tumours (Riva & Giorgi, 2000)

	Right (n=7)	Left (n=8)	Midline (n=6)
VIQ	-1.4	+0.2	+0.6
PIQ	+0.3	-1.3	+0.06
Lexical naming	-1.5	-1.4	-0.5
Lexical comprehension	-1.3	-1.9	-0.2
Token Test	-1.6	+1.4	-0.5
MLU	-2.3	+1.4	-0.23
Visual sequential memory	+0.8	-1.7	+1.8
Auditory sequential memory	-1.8	+1.2	+0.4
WCST (perseverations)	+2.5	+2.1	+1.27
Design fluency	ND	-2.4	-2.08
Verbal fluency	-2.9	-1.7	-2.93
Attention	**-3.1**	**-3.2**	**-2.97**

Conclusions

- Impairments in attention and executive function are an important part of the co-morbidity of neurological diseases.
- ADHD is almost certainly under-recognised and as such is often under-treated
- There is limited evidence to guide the treatment for children with neurological disorders and ADHD