Cognition in Childhood Epilepsy: Is there a typical cognitive phenotype in childhood epilepsy?

Colin Reilly, Educational Psychologist
Young Epilepsy

Mind the Gap V symposium
November 12th 2015
Childhood Epilepsy

- The childhood epilepsies comprise a heterogeneous group of disorders and syndromes that vary in terms of severity, prognosis and treatment requirements (Cross et al. 2013).
- Epilepsy should be understood as a **Disability Complex** (Neville, 1999) - Epileptic Seizures **and** an increased risk for:
  - **Cognitive difficulties** (Global or Specific)
  - Symptoms of **Neurodevelopmental Disorders** – ADHD and ASD
  - Symptoms of **Emotional Disorders** (Anxiety and Depression)
  - A range of **motor difficulties** including DCD
  - **Academic Underachievement**
- Cognitive profiles in epilepsy are as heterogeneous as the epileptic syndromes themselves (Elger et al. 2004)
Cognition and Epilepsy

- Prevalence of global cognitive difficulties
- Prevalence of specific cognitive difficulties
- Correlates of cognitive difficulties
- Population-based - cognition in ‘Active Epilepsy’ – The CHESS study
- Supporting children with cognitive difficulties
- Core deficits and neurobiology?
- Conclusion - a cognitive phenotype?
Global Cognition in Childhood Epilepsy

• Reported rates of Intellectual developmental disorder (IDD) in children with epilepsy range from 21% to 40%\(^1\).

• Berg et al. (2008) (n=584).
  – 73.6% had ‘normal’ (IQ ≥ 80), 26.4% had ‘subnormal’ functioning (IQ less than 80) and 21.3% had ID (IQ < 70)

• 43% of children with epilepsy scored < 10\(^{th}\) percentile on Ravens compared with 3% controls (Høie et al. 2005)

\(^1\) Berg et al. (2008), Murphy et al. (1995), Ellenberg et al. (1984), Steffenberg et al. (1995).
Factors significantly associated with Global Cognitive impairment in Childhood Epilepsy

• What drives the cognitive impairment:
  – Underlying developmental/neurological substrate?
  – The effect of seizures/epileptic activity?
  – Effects of AEDs?

• Global Cognitive impairment associated with:
  – Early Age of Onset
  – Aetiology of epilepsy –symptomatic/structural cause
  – Presence of Epileptic Encephalopathy
  – Current Treatment status
  – Drug resistance
  – Seizure Frequency
  – Duration?

Memory in Childhood Epilepsy

• 78% of studies - children with epilepsy scored lower than controls and normative scores (Menlove et al. 2014)

• Impairments compared to controls and normative scores in:
  – Visual memory tasks (Nolan et al. 2004)
  – Delayed Recall /Long-term memory (Davidson et al. 2007; Gascoigne et al. 2012).
  – Episodic, semantic and phonological memory (Rzezak et al. 2011; Smith & Lae, 2011)
  – Memory for emotions (Jambaqué et al. 2009; Pinabiaux et al. 2013)

• Neurocognitive deficits present in the context of grossly intact global intellectual functioning in children with epilepsy (Kernan et al. 2012)
Processing Speed in Childhood Epilepsy

• Berg et al. (2008) reported that full-scale IQ scores lower for children with uncomplicated idiopathic or cryptogenic epilepsy compared with siblings mainly due to slower processing speed (Wechsler tests).

• Hermann et al. (2006); recently diagnosed epilepsy- psychomotor function, measured in part via coding subtest from WISC was most affected.

• Sherman et al. (2012) – lowest mean score on processing speed index of WISC-IV and coding lowest
Trajectory of Cognitive Development

• Rathouz et al. (2014)
  – Cognitive deficits present at or near time of diagnosis and no progressive deterioration in Idiopathic Generalised Epilepsy (6 year follow-up)

• Oostrom et al. (2005) (Idiopathic and Cryptogenic)
  – No changes in cognition over time, but instability in individual performances appeared to characterize children with epilepsy only.
The Children with Epilepsy in Sussex Schools (CHESS) study

- All school-aged children (4-15 years) with ‘active epilepsy’ (on one or more Anti Epileptic Drug (AED) and/or had a seizure in the last year) in a defined area in West Sussex UK.

- Prevalence of ‘Active’ epilepsy was 1 in 286 and Lifetime epilepsy was 1 in 175 (Total population 202,919)

- 85 children (74% of eligible population) underwent comprehensive psychological assessment
  - Cognition and screening measures for ASD, ADHD, Developmental Coordination Disorder (DCD), Depression and Anxiety.
## Global Cognition - Instruments

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Instrument</th>
<th>Low-Functioning Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 years</td>
<td>Stanford Binet Intelligence Scales - Fifth Edition (SB-V) (n=4)</td>
<td>Griffiths Mental Development Scale –Extended Revised (GMDS-ER) (n=3)</td>
</tr>
<tr>
<td>6-15 years</td>
<td>Wechsler Abbreviated Scale of Intelligence (WASI) (n=61)</td>
<td>GMDS-ER (n=13) or SB-V (n=4)</td>
</tr>
</tbody>
</table>
## Memory and Processing Speed

<table>
<thead>
<tr>
<th>Test: Subtest</th>
<th>Score Used</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Working Memory Battery- Children (WMTB-C)</strong></td>
<td>Standard Scores $M=100$ $SD=15$</td>
</tr>
<tr>
<td>Digit Recall</td>
<td></td>
</tr>
<tr>
<td>Block Recall</td>
<td></td>
</tr>
<tr>
<td>Backward Digit Recall</td>
<td></td>
</tr>
<tr>
<td>Counting Recall</td>
<td></td>
</tr>
<tr>
<td><strong>Wechsler Intelligence Battery for Children (WISC-IV)</strong></td>
<td>PSI $M=100$ $SD=15$ Subtest Scaled Scores $M=10$ $SD=3$</td>
</tr>
</tbody>
</table>
Figure 1: Distribution of IQ scores in CHESS study

<table>
<thead>
<tr>
<th></th>
<th>Above Average (115+)</th>
<th>Average (85-114)</th>
<th>Borderline (70-84)</th>
<th>Mild (50-69)</th>
<th>Moderate (35-49)</th>
<th>Severe-Profound (0-34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VIQ</td>
<td>6</td>
<td>33</td>
<td>12</td>
<td>14</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>PIQ</td>
<td>3</td>
<td>35</td>
<td>16</td>
<td>10</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>FSIQ</td>
<td>3</td>
<td>35</td>
<td>13</td>
<td>14</td>
<td>4</td>
<td>16</td>
</tr>
</tbody>
</table>
Global Cognitive Functioning

<table>
<thead>
<tr>
<th>Score Range</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>120+</td>
<td>1</td>
</tr>
<tr>
<td>110-119</td>
<td>6</td>
</tr>
<tr>
<td>90-109</td>
<td>24</td>
</tr>
<tr>
<td>85-89</td>
<td>7</td>
</tr>
<tr>
<td>70-79</td>
<td>13</td>
</tr>
<tr>
<td>Mild (50-69)</td>
<td>14</td>
</tr>
<tr>
<td>Mod (35-49)</td>
<td>4</td>
</tr>
<tr>
<td>Sev-Prof (0-34)</td>
<td>16</td>
</tr>
</tbody>
</table>
Wechsler Subtest Scores

<table>
<thead>
<tr>
<th>Subtest</th>
<th>VOC</th>
<th>BD</th>
<th>SIM</th>
<th>MR</th>
<th>CD</th>
<th>SS</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHESS Scores</td>
<td>7.56</td>
<td>7.82</td>
<td>8.01</td>
<td>7.48</td>
<td>5.92</td>
<td>6.98</td>
</tr>
<tr>
<td>SUBTEST MEAN</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>
WMTB-C Subtest Scores

![Graph showing WMTB-C Subtest Scores]

- Forward Digit Span
- Block Recall
- Backwards Digit Span
- Counting Recall

Lines represent:
- Blue: CHESS Memory scores
- Red: Mean Memory Scores
- Green: CHESS IQ SCORE
Specific Aspects of Cognition

• 58% of children had ‘memory underachievement’ (Memory score 1SD below their assessed IQ score in at least one of the four subtests). 36% had underachievement on two or more tests.

• Processing Speed Index Scores significantly lower than PIQ or VIQ (p<.001)

• Coding subtest particularly low and significantly lower than all the other Wechsler tests (p<.05) - The Coding subtest measures - short-term nonverbal memory, short-term learning of nonverbal symbols, visual perception and fine-motor coordination.
Neurobehavioral Impairments in CHESS Study

- Cog. Imp.: 55%
- IDD: 40%
- ADHD: 33%
- ASD: 21%
- DCD: 19%
- Anxiety: 13%
- Depression: 7%
Predictors of IDD on multivariable analysis in CHESS study

- Seizures before 24 months
- Being on polytherapy
- Having ASD
- Having predominantly generalized seizures
- Having experienced at least one episode of status epilepticus.
Age of onset of Epilepsy

<table>
<thead>
<tr>
<th>Age Category of First seizure</th>
<th>Non IDD</th>
<th>IDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-24months</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>25-60 months</td>
<td>20</td>
<td>8</td>
</tr>
<tr>
<td>61 months or more</td>
<td>25</td>
<td>6</td>
</tr>
</tbody>
</table>
Supporting Children with Global Cognitive Impairments

• Accurate assessment of level of functioning and child’s profile enhances understanding for child, parents and school staff.
  – 11/24 children not on special educational needs register (SEN) had global cognitive impairment and/or had a DSM-IV disorder
  – 15/24 of children not on SEN register had memory underachievement in at least one area and 10/24 had a problem on more than one subtest

• Accommodations may be needed
  – Extra Time for examinations, Classroom accommodations, Memory Strategies

• Remediating/Rehabilitation?
Interventions?

• Memory rehabilitation - mixed results (Koorenhof et al. 2012)
  • Cogmed working memory training - positive initial data in epilepsy (Westerberg et al. 2006: Berl et al. 2014 and Kerr and Blackwell, 2015 study)
  • But lack of generalization and gains not sustained (Melby-Lervåg & Hulme, 2013).

• Environmental enrichment for cognition?
  • Animal models (e.g. Bender et al. 2013)
Consequences of Cognitive Impairments in Childhood Epilepsy

- Global cognitive impairment is significantly associated with lowered quality of life (Reilly et al. 2015)

- Global cognitive impairment is significantly associated with lower scores on academic achievement (Reilly et al. 2014)

- Combined health care, social care, and education costs were significantly related to cognitive impairment (intelligence quotient [IQ] < 85) and seizure frequency (p < 0.05). (Hunter et al. 2015)
Core cognitive deficits in Childhood epilepsy?

- What is most affected and what is relatively spared in those without IDD in childhood epilepsy?
  - Most affected:
    - Memory, attention, psychomotor speed?
  - Relatively Spared:
    - Core verbal and performance?
**ADHD-RS-IV Inattention subscale percentiles**

<table>
<thead>
<tr>
<th>Parent</th>
<th>0-24th</th>
<th>25th-49th</th>
<th>50th-74th</th>
<th>75th-100th</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0%</td>
<td>10%</td>
<td>13%</td>
<td>77%</td>
</tr>
</tbody>
</table>

Percentage of children
Neurobiology?

- Epilepsy interferes with the developmental trajectory of brain networks underlying cognition and it would appear that the underlying aetiology of a child’s epilepsy is involved in the mechanism of permanent deficits in cognition.

- This underlying aetiology contributes to the generation of seizures as well as lasting changes in neural circuits affecting the brains’ ability to process and store information.

- How changes in neural circuitry contribute to memory or other cognitive processes is not clear. It is also not clear if different aetiologies, different types of seizures or different medications affect cognitive processes in a different manner.
Conclusion

• Global and specific cognitive impairments are features across the epilepsies

• Cognitive Phenotype?:
  – Processing Speed deficits are very common - likely to be a mix of psychomotor and broader level cognitive problems
  – Memory difficulties and symptoms of ADHD (Particularly inattention) very common - Difficulties with executive functioning?

• Children’s global difficulties will be identified but specific deficits less likely.

• We need to identify ways to lessen impact of cognitive difficulties on school performance by developing efficacious interventions to improve specific and global? aspects of cognitive functioning.

• Children with epilepsy need cognitive screening (Wilson, 2015) but what does screening mean and are the resources currently in place?