Learning disabilities in children with epilepsy
Causes and consequences

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4th EMEC
Academic achievement in CWE

• Academic achievement across different chronic childhood conditions:
  – indicates that children with epilepsy are one of the most vulnerable groups

• About 50% of CWE have school-related difficulties:
  – one third of them needs additional academic support vs 7% in a matched non neurological chronic disease

• Only 33% (vs 68% in general population) of CWE between 12 and 18 years are in the secondary school

Aldenkamp AP, 1990, 2005; Bulteau, 2000
Burden of the situation

• Epilepsy is a frequent chronic disease with variable etiology:
  – One per cent of children will develop epilepsy by 20 years of age
• As a brain disease, significant complication of epilepsy is:
  – the high risk for impairment in global or specific aspects of cognition
• Indeed, in childhood, epilepsy can interfere with brain development and interfere the underlying neural networks:
  – resulting in major global or specific cognitive disorders

Hauser, 1994; Cowan LD, 2002
COGNITIVE FUNCTION IN CWE
Cognitive deficits in CWE

• Global cognitive deficit:
  – Intellectual disabilities
    • IQ<70

• Selective cognitive deficit:
  – Learning difficulties
    • In children with intellectual disabilities
    • But also in children with IQ>80
Global cognitive deficit in CWE

- Global cognition function was considered abnormal and IQ < 70 in:
  - Ellenberg et al, 1984: 27%
  - Murphy et al, 1995: 30%
  - Campfield et camfield, 2003: 32%
  - Berg et al, 2008: 21.3%
  - Reiley et al, 2014: 40%

- Level of cognitive function (IQ):
  - Mild (IQ scores of 60-69): 3.4%
  - Moderately or severely (IQ scores of <60): 7.3%
  - Neurologically devasted: 4.7%
  - Impaired-NFC: 5.9%

Berg, 2008; Reiley, 2014, 2015
IQ distribution and school placement

Bulteau C, 2000
## Global cognitive function in children with epilepsy: A community-based study

*Anne T. Berg, †John T. Langfitt, ‡Francine M. Testa, §§Susan R. Levy, ¶Francis DiMario, #Michael Westerveld, and ¶¶Joseph Kulas

### Table 1. Association of age at onset, etiology, syndrome group, remission status, and AED status with cognitive function

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Within Normal</th>
<th>Borderline</th>
<th>Mild MR</th>
<th>MR</th>
<th>Devastated</th>
<th>Impaired-NFC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at onset</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>&lt;5 years</td>
<td>281</td>
<td>166 (59.1%)</td>
<td>21 (7.5%)</td>
<td>11 (3.9%)</td>
<td>31 (11.0%)</td>
<td>24 (8.5%)</td>
<td>28 (10.0%)</td>
</tr>
<tr>
<td>5–9 years</td>
<td>225</td>
<td>192 (85.3%)</td>
<td>8 (3.6%)</td>
<td>6 (2.7%)</td>
<td>10 (4.4%)</td>
<td>2 (0.9%)</td>
<td>7 (3.1%)</td>
</tr>
<tr>
<td>≥10 years</td>
<td>107</td>
<td>93 (86.9%)</td>
<td>2 (1.9%)</td>
<td>4 (3.7%)</td>
<td>4 (3.7%)</td>
<td>3 (2.8%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td><strong>Etiology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Idiopathic/cryptogenic</td>
<td>473</td>
<td>401 (84.8%)</td>
<td>25 (5.3%)</td>
<td>14 (3.0%)</td>
<td>9 (1.9%)</td>
<td>3 (0.6%)</td>
<td>21 (4.5%)</td>
</tr>
<tr>
<td>Symptomatic/secondarya</td>
<td>140</td>
<td>50 (35.7%)</td>
<td>6 (4.3%)</td>
<td>7 (5.0%)</td>
<td>36 (25.7%)</td>
<td>26 (18.6%)</td>
<td>15 (10.7%)</td>
</tr>
<tr>
<td><strong>Syndrome groupb</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ILRE</td>
<td>71</td>
<td>67 (93.4%)</td>
<td>3 (4.2%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>SFE</td>
<td>97</td>
<td>45 (46.4%)</td>
<td>6 (6.2%)</td>
<td>5 (5.2%)</td>
<td>26 (26.8%)</td>
<td>6 (6.2%)</td>
<td>9 (9.3%)</td>
</tr>
<tr>
<td>CFE</td>
<td>208</td>
<td>181 (87.0%)</td>
<td>13 (6.3%)</td>
<td>9 (4.3%)</td>
<td>0</td>
<td>0</td>
<td>5 (2.4%)</td>
</tr>
<tr>
<td>IGE</td>
<td>131</td>
<td>113 (86.3%)</td>
<td>6 (4.6%)</td>
<td>4 (3.1%)</td>
<td>0</td>
<td>0</td>
<td>8 (6.1%)</td>
</tr>
<tr>
<td>Undetermined</td>
<td>38</td>
<td>31 (81.6%)</td>
<td>1 (2.6%)</td>
<td>0</td>
<td>1 (2.6%)</td>
<td>1 (2.6%)</td>
<td>4 (10.5%)</td>
</tr>
<tr>
<td>Nonepileptic encephalopathies combined (ILRE-undetermined)</td>
<td>545</td>
<td>437 (80.2%)</td>
<td>29 (5.3%)</td>
<td>18 (3.3%)</td>
<td>27 (5.0%)</td>
<td>7 (1.3%)</td>
<td>27 (5.0%)</td>
</tr>
<tr>
<td>Epileptic encephalopathy</td>
<td>68</td>
<td>14 (20.6%)</td>
<td>2 (2.9%)</td>
<td>3 (4.4%)</td>
<td>18 (26.5%)</td>
<td>22 (32.4%)</td>
<td>9 (13.2%)</td>
</tr>
<tr>
<td><strong>Remission status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5 years seizure free</td>
<td>246</td>
<td>148 (60.2%)</td>
<td>15 (6.1%)</td>
<td>14 (5.7%)</td>
<td>33 (13.4%)</td>
<td>19 (7.7%)</td>
<td>17 (6.9%)</td>
</tr>
<tr>
<td>≥5 years seizure free</td>
<td>320</td>
<td>277 (86.6%)</td>
<td>15 (4.7%)</td>
<td>7 (2.2%)</td>
<td>10 (3.1%)</td>
<td>1 (0.3%)</td>
<td>10 (3.1%)</td>
</tr>
<tr>
<td>Followed &lt;5 yearsc</td>
<td>47</td>
<td>26 (55.3%)</td>
<td>1 (2.1%)</td>
<td>0</td>
<td>2 (4.3%)</td>
<td>9 (19.2%)</td>
<td>9 (19.2%)</td>
</tr>
<tr>
<td><strong>AED status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No AEDs</td>
<td>357</td>
<td>308 (86.3%)</td>
<td>17 (4.8%)</td>
<td>6 (1.7%)</td>
<td>10 (2.8%)</td>
<td>2 (0.6%)</td>
<td>14 (3.9%)</td>
</tr>
<tr>
<td>Taking ≥1 AED</td>
<td>256</td>
<td>143 (55.9%)</td>
<td>14 (5.5%)</td>
<td>15 (5.9%)</td>
<td>35 (13.7%)</td>
<td>27 (10.6%)</td>
<td>22 (8.6%)</td>
</tr>
</tbody>
</table>
IQ distribution and school placement

- Among CWE in mainstream school, 20 to 70% had school difficulties

Bulteau C, 2000
Cognitive deficits in CWE

• Global cognitive deficit:
  – Intellectual disabilities

• Selective cognitive deficit:
  – Speed of information processing
  – Memory
  – Vigilance, alertness
  – Sustained and focused attention
  – Motorfluency
Cognition in school-aged children with “active” epilepsy: A population-based study

Colin Reilly\textsuperscript{ac}, Patricia Atkinson\textsuperscript{b}, Krishna B. Das\textsuperscript{aeef}, Richard F. M. Chin\textsuperscript{g}, Sarah E. Aylett\textsuperscript{ef}, Victoria Burch\textsuperscript{a}, Christopher Gillberg\textsuperscript{ce}, Rod C. Scott\textsuperscript{def} & Brian G. R. Neville\textsuperscript{ae}

### Mean FSIQ, VIQ, and PIQ scores

<table>
<thead>
<tr>
<th>IQ scale</th>
<th>Mean</th>
<th>Range</th>
<th>SD</th>
<th>(&lt;1 SD)</th>
<th>(&gt;2 SDs)</th>
<th>(&lt;2 SDs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VIQ</td>
<td>86.94</td>
<td>43–140</td>
<td>22.64</td>
<td>17</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>PIQ</td>
<td>84.51</td>
<td>42–123</td>
<td>19.35</td>
<td>23</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>FSIQ</td>
<td>84.96</td>
<td>40–120</td>
<td>20.70</td>
<td>22</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>PSI\textsuperscript{a}</td>
<td>79.45</td>
<td>50–126</td>
<td>18.48</td>
<td>37</td>
<td>25</td>
<td></td>
</tr>
</tbody>
</table>

**Note.** \(N = 69\). Including Stanford Binet Intelligence Scale—Fifth Edition (SB–V) scores. VIQ = Verbal IQ; PIQ = Performance IQ; FSIQ = full-scale IQ; PSI = Processing Speed Index.

\(n = 60\).

### Scores on subtests of the Wechsler subtests

<table>
<thead>
<tr>
<th>Wechsler subtest</th>
<th>Mean</th>
<th>Range</th>
<th>SD</th>
<th>(&lt;1 SD)</th>
<th>(&gt;2 SDs)</th>
<th>(&lt;2 SDs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vocabulary</td>
<td>7.56</td>
<td>1–17</td>
<td>4.52</td>
<td>17</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>Block Design</td>
<td>7.82</td>
<td>3–14</td>
<td>2.90</td>
<td>33</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Similarities</td>
<td>8.08</td>
<td>1–17</td>
<td>3.95</td>
<td>25</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Matrix Reasoning</td>
<td>7.48</td>
<td>1–16</td>
<td>3.85</td>
<td>30</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td><strong>Coding\textsuperscript{a}</strong></td>
<td>5.92</td>
<td>1–16</td>
<td>3.15</td>
<td><strong>37</strong></td>
<td><strong>32</strong></td>
<td></td>
</tr>
<tr>
<td>Symbol Search\textsuperscript{a}</td>
<td>6.82</td>
<td>1–15</td>
<td>4.06</td>
<td>20</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>

**Note.** \(N = 61\). Subtest mean score = 10, range = 1–19 and \(SD = 3\) in normative samples.

\(n = 60\).
Memory

- Relative difficulties in working memory are very common in pediatric epilepsy

<table>
<thead>
<tr>
<th>Subtest standard score</th>
<th>Mean</th>
<th>Range</th>
<th>SD</th>
<th>≥1 SD below FSIQ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digit Recall</td>
<td>82.76</td>
<td>55–137</td>
<td>17.49115</td>
<td>29</td>
</tr>
<tr>
<td>Block Recall</td>
<td>83.86</td>
<td>55–113</td>
<td>17.47164</td>
<td>17</td>
</tr>
<tr>
<td>Backwards Digit Recall</td>
<td>81.11</td>
<td>55–121</td>
<td>16.21123</td>
<td>34</td>
</tr>
<tr>
<td>Counting Recall(^a)</td>
<td>78.72</td>
<td>55–127</td>
<td>19.02168</td>
<td>35</td>
</tr>
</tbody>
</table>

Note. N = 66. FSIQ = full-scale IQ; WMTB-C = Working Memory Test Battery for Children.

\(^a\)n = 64.
Factors associated with cognitive deficit

<table>
<thead>
<tr>
<th>Domain</th>
<th>n</th>
<th>Factors</th>
<th>B [95% CI]</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FSIQ</strong></td>
<td>69</td>
<td>Sz. onset (&lt;24 mths vs. ≥24 mths)</td>
<td>-11.21 [-1.44, -20.97]</td>
<td>.025</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monotherapy vs. polytherapy</td>
<td>-14.89 [-23.57, -6.22]</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ADHD</td>
<td>-11.14 [-3.03, -19.25]</td>
<td>.008</td>
</tr>
<tr>
<td><strong>Work. Memory Comp.</strong></td>
<td>66</td>
<td>Monotherapy vs. polytherapy</td>
<td>-13.00 [-19.30, -6.60]</td>
<td>.000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Generalized vs. focal seizures</td>
<td>-6.99 [-0.37, -13.60]</td>
<td>.039</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ADHD</td>
<td>-7.24 [-1.10, -13.38]</td>
<td>.022</td>
</tr>
<tr>
<td><strong>PSI</strong></td>
<td>61</td>
<td>Sz. onset (&lt;24 mths vs. ≥24 mths)</td>
<td>-11.64 [-2.42, -20.87]</td>
<td>.014</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monotherapy vs. polytherapy</td>
<td>-12.83 [-20.41, -5.26]</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ADHD</td>
<td>-8.77 [-1.47, -16.06]</td>
<td>.019</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DCD</td>
<td>-12.65 [-4.95, -20.36]</td>
<td>.002</td>
</tr>
</tbody>
</table>

Note. FSIQ = full-scale IQ; work. memory comp. = working memory composite; PSI = Processing Speed Index; CI = confidence interval; Sz. = seizure; mths = months; ADHD = attention-deficit/hyperactivity disorder; DCD = developmental coordination disorder.

p > .05.

Reiley et al, 2015
ADHD

• ADHD has been identified as one of the essential comorbidities influencing academic performance of CWE
• The prevalence is between 14% to 38% of CWE
• There is no formal correlation between the severity of ADHD and:
  - the duration of epilepsy
  - the seizure frequency
  - the ongoing antiepileptic drug.
• The use of MPH decrease ADHD symptoms in 75% of treated patients without significant relapse of seizures

Rheims S, 2016
Attention deficits in CWE

• Problems with attention are a common clinical complaint among CWE
• The pattern of impaired and preserved attentional skills may be determined by certain epilepsy variables
• Attention deficits have been observed in focal and idiopathic generalized epilepsy
• Seizures frequency has been correlated with parent-reported attention problems
• Some antiepileptics may worsen attention deficit disorders

Gascoigne, 2017
Specific learning disabilities

- LDs are defined as disorders that interfere with academic performance in subjects with normal IQ.
- LDs are considered to be one of the most important factors leading to poor academic outcome.
- Up to 25% of PWE have LD and up to 50% of people with LD have epilepsy:
  - Dyslexia 13 to 32%
  - Dysgraphia 35 to 56%
  - Dyscalculia 20 to 38%

Sillanppää 1992, 2004; Beghi M, 2006; Fastenau, 2008; Pavlou, 2011
FACTORS WITH DETRIMENTAL EFFECTS ON COGNITION AND LEARNING
Cognitive difficulties in PWE

• Chronic cognitive impairments are caused by brain lesion and/or stable brain dysfunction

• Dynamic cognitive impairment:
  – Recurrent seizures
  – Epileptiform abnormalities
  – Effects of AED

• Dynamic cognitive deficits can become permanent if:
  – the negative impact of the transient changes are not or cannot be ameliorated
  – the dynamic changes occur during critical periods of development such as sleep or early development

Kleen et al., 2012; Colin R et al, 2015
Underlying disorders/seizures

• ID is more associated with:
  – abnormal brain imaging (64.5% of children)
  – Genetic, metabolic or neurodegenerative disorders

• Onset of seizures at an early age:
  – Before 24 months

• Seizure type:
  – GTC and focal seizures with impaired awareness

• Time of occurrence:
  – Diurnal seizures: information processing system
  – Nocturnal seizures: language functions, memory, alertness

Aldenkamp, 1990; Berg, 2009; Gulati, 2014
Epileptiform EEG/localization of epileptogenic foci

• Epileptiform EEG:
  – focal interictal spikes transiently disrupt aspects of cortical functioning corresponding to their neuroanatomical location

• Localization of epileptogenic foci:
  – Temporal lobe epilepsy: memory deficiency
  – Frontal lobe epilepsy: attention and memory deficit

• Lateralisaton
  – left hemisphere: verbal learning, verbal memory, and serial information processing.
  – right hemispheric: visual-spatial tasks
Effects of AED

• Phenobarbitone has the maximum detrimental effect on cognition followed by valproate, carbamazepine and phenytoin, the latter three having similar effect.

• Lamotrigine has no effect on cognition.

• In epileptic patients, topiramate had an effect on memory and on word fluency, verbal processing and verbal IQ.

Lee 2002, 2003; Aldenkamp, Pavlou, 2011
MANAGEMENT OF LD IN CWE
Management of LD in CWE

• Initiate early effective treatment
• Polytherapy:
  – reduction of the number of AED
• Best choice for AED:
  – Avoid AED with sedative and cognitive effect
• In case of ADHD:
  – use of methylphenidate
• Specific educational Therapy
• Teaching assistants
• Stable and healthy family and school environment
Tunisian National Epilepsy Day

9-11 February 2017
Sfax Tunisia