Early Prediction of Outcome in Compromised Term and Preterm Infants

Professor Lena Hellström-Westas, MD PhD
Department of Women’s and Children’s Health
Uppsala University and University Hospital, Sweden
Lena.westas@kbh.uu.se
Objective:
To review major features and findings in the aEEG and EEG that are associated with prognosis in newborn infants
Why is the possibility to predict outcome important in the NICU?

**Short-term/Acute**
- Guide acute medical investigations and treatments
- Inform parents
  - Examples: Decision on hypothermia treatment, direct further investigations and treatment, assess infants at high risk of seizures

**Long-term**
- Guide further medical investigations and treatments
- Inform parents
  - Examples: Follow up strategies, e.g. do MRI, physiotherapy, prophylactic antiepileptic treatment
EEG background abnormality correlates with severity of brain injury (Aso et al, J Clin Neurophysiol 1989)
The aEEG/EEG responses to an acute insult are:
- Consistent and predictable
- Correlate with the severity of brain injury
- Similar responses in adults, infants, and animals

(Watanabe et al, Brain Dev 1999)
aEEG for prediction of outcome in full-term infants

Asphyxiated infants

- Background activity
  - at 6h predicts outcome in 90%
  - at 3h predicts outcome in 70-80%
  - Meta-analysis of 8 studies: sens 91%, spec 88% for predicting disability/death
    (Spitzmiller et al, J Child Neurol 2007)

- Sleep-wake cycling (SWC) at 36-48 h = better outcome

- Seizures – markers of injury

- Congenital heart disease
  - Suppressed or no SWC first 48 h after surgery = poorer IQ at 4 years
    (Latal et al, J Pediatr 2016)
Hypothermia changes the predictive value of the aEEG
N=43 cooled and N=31 non-cooled infants
(Thoresen et al, Pediatrics 2010)

Predictive value of amplitude-integrated EEG (aEEG) after rescue hypothermic neuroprotection for hypoxic ischemic encephalopathy: a meta-analysis
M Chandrasekaran\textsuperscript{1,2}, B Chaban\textsuperscript{1}, P Montaldo\textsuperscript{1} and S Thayyil\textsuperscript{1}

Included 9 studies (520 infants). The pooled sensitivity/specificity at 6 h for an abnormal trace to predict poor outcome was 96%/39%. The predictive value was best at 48 h with an odds ratio for a poor trace to predict poor outcome of 66.9 (95%CI 19.7-227.2)
Early sleep-wake cycling (SWC) and outcome in asphyxiated term infants

Normothermia
• SWC <36 h = better outcome (+8.5 Griffith DQ); outcome correctly predicted in 82% at 36 h (Osredkar et al, Pediatrics 2005)

Hypothermia - delayed SWC
• SWC at 48-60 h ~ good outcome (Thoresen et al, Pediatrics 2010)
• SWC day 1 or 2 = 100% PPV good outcome (Massaro et al, Neonatology 2012)
Seizure burden during hypothermia is associated with severity of brain injury (Shah et al ADFCN 2013)

N= 85 hypothermia-treated neonates; 52% had seizures on aEEG/EEG (35% had high seizure burden), 49% had abnormal aEEG background in the first 24 h and 36% had severe injury on MRI.

Multivariate regression model assessing the effect of factors significant in above bivariate analyses on MRI outcomes

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR</th>
<th>Lower CI</th>
<th>Upper CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure burden</td>
<td>5.00</td>
<td>1.47</td>
<td>17.05</td>
<td>0.01</td>
</tr>
<tr>
<td>Apgar at 10 min</td>
<td>0.80</td>
<td>0.59</td>
<td>1.10</td>
<td>0.18</td>
</tr>
<tr>
<td>Abnormal aEEG background in first 24 h</td>
<td>2.30</td>
<td>0.50</td>
<td>10.51</td>
<td>0.28</td>
</tr>
<tr>
<td>aEEG background at 48 h</td>
<td>2.55</td>
<td>0.48</td>
<td>13.54</td>
<td>0.27</td>
</tr>
</tbody>
</table>

Injury on MRI
Black= severe
Grey=non-severe
EEG background features that predict outcome in term neonates with hypoxic ischaemic encephalopathy: A structured review

Md. Abdul Awal a,b,*, Melissa M. Lai a,b, Ghasem Azemi c, Boualem Boashash d,b,a, Paul B. Colditz a,b

N=31 studies, January 1960-April 2014

Pooled sensitivity and specificity with confidence interval for different EEG background patterns.

<table>
<thead>
<tr>
<th>EEG background patterns</th>
<th>No. of studies</th>
<th>No. of neonates</th>
<th>Pooled sensitivity</th>
<th>Pooled specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Point estimate</td>
<td>95% CI</td>
</tr>
<tr>
<td>Burst suppression</td>
<td>29</td>
<td>914</td>
<td>0.87</td>
<td>0.78–0.92</td>
</tr>
<tr>
<td>Low voltage</td>
<td>19</td>
<td>566</td>
<td>0.92</td>
<td>0.72–0.98</td>
</tr>
<tr>
<td>Flat trace</td>
<td>13</td>
<td>493</td>
<td>0.78</td>
<td>0.58–0.91</td>
</tr>
</tbody>
</table>

Burst suppression

(a)

Low voltage

(b)

Flat trace

(C)
EEG background features that predict outcome in term neonates with hypoxic ischaemic encephalopathy: A structured review

Md. Abdul Awal\textsuperscript{a,b,*}, Melissa M. Lai\textsuperscript{a,b}, Ghasem Azemi\textsuperscript{c}, Boualem Boashash\textsuperscript{d,b,a}, Paul B. Colditz\textsuperscript{a,b}

N=31 studies, January 1960-April 2014

Pooled sensitivity and specificity with confidence interval for different EEG background patterns.

<table>
<thead>
<tr>
<th>EEG background patterns</th>
<th>No. of studies</th>
<th>No. of neonates</th>
<th>Pooled sensitivity</th>
<th>Pooled specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Point estimate</td>
<td>95% CI</td>
</tr>
<tr>
<td>Burst suppression</td>
<td>29</td>
<td>914</td>
<td>0.87</td>
<td>0.78–0.92</td>
</tr>
<tr>
<td>Low voltage</td>
<td>19</td>
<td>566</td>
<td>0.92</td>
<td>0.72–0.98</td>
</tr>
<tr>
<td>Flat trace</td>
<td>13</td>
<td>493</td>
<td>0.78</td>
<td>0.58–0.91</td>
</tr>
</tbody>
</table>
### EEG background features that predict outcome in term neonates with hypoxic ischaemic encephalopathy: A structured review

Md. Abdul Awal\textsuperscript{a,b,*}, Melissa M. Lai\textsuperscript{a,b}, Ghasem Azemi\textsuperscript{c}, Boualem Boashash\textsuperscript{d,b,a}, Paul B. Colditz\textsuperscript{a,b}

N=31 studies, January 1960-April 2014

(Pooled sensitivity and specificity with confidence interval for different EEG background patterns.)

<table>
<thead>
<tr>
<th>EEG background patterns</th>
<th>No. of studies</th>
<th>No. of neonates</th>
<th>Pooled sensitivity</th>
<th>Pooled specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Point estimate</td>
<td>95% CI</td>
</tr>
<tr>
<td>Burst suppression</td>
<td>29</td>
<td>914</td>
<td>0.87</td>
<td>0.78–0.92</td>
</tr>
<tr>
<td>Low voltage</td>
<td>19</td>
<td>566</td>
<td>0.92</td>
<td>0.72–0.98</td>
</tr>
<tr>
<td>Flat trace</td>
<td>13</td>
<td>493</td>
<td>0.78</td>
<td>0.58–0.91</td>
</tr>
</tbody>
</table>

**Burst suppression**

(a)

**Low voltage**

(b)

**Flat trace**

(C)
Prediction of outcome in asphyxiated moderately preterm infants?

Placental abruption at 34+4 w, BW 1780 g, "HIE 2", day 1-2, Outcome at 2 years: CP and mental retardation
Jiang et al (Eur J Paediatr 2015)

N=170 asphyxiated late preterm infants (GA 34-36 w) who survived to BSID-II at 18 months. Predictive value of aEEG at 6 hours postnatal age – in relation to adverse neurological outcome: Sens 81%, Spec 92%, 90% correctly predicted

Prognosis in this infant - born at GA 33 w after placental abruption (day 1)?
aEEG background and lower border correlates with severity of brain injury in infants with NE (Shah et al, Pediatrics 2006)

N=86 term infants with neonatal encephalopathy (NE):
Causes: 40 HIE, 10 infection, 10 seizures, 9 vascular, 5 pulmonary, 5 maternal drug, 4 metabolic, 3 syndrome
A severely abnormal aEEG predicted adverse neurological outcome with sensitivity 70.2%, specificity 87.1%, PPV 75.6% and NPV 83.7%.
Early Amplitude-Integrated Electroencephalography Predicts Long-Term Outcomes in Term and Near-Term Newborns With Severe Hyperbilirubinemia

(Yuan et al, Pediatr Neurol 2020)

83 individuals

GA ≥35 w, TSB ≥340µmol/L/19.9 mg/dL, or TSB ≥257µmol/L/15 mg/dL and BIND

77 eligibility

2 moderate to severe HIE
2 purulent meningitis
1 grade III intracranial hemorrhage
1 congenital brain abnormality

Underwent aEEG, MRI, and/or ABR

33 ABE

44 severe hyperbilirubinemia

13 lost to follow up

2 died of ABE
12 adverse outcome
50 favorable outcome

BSID-II at 12 months

Predictive Values of aEEG and ABR

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severely abnormal aEEG</td>
<td>35.7</td>
<td>92.0</td>
<td>55.6</td>
<td>83.6</td>
<td>79.7</td>
</tr>
<tr>
<td>Abnormal ABR</td>
<td>83.3</td>
<td>74.1</td>
<td>58.8</td>
<td>90.9</td>
<td>76.9</td>
</tr>
</tbody>
</table>
EEG and aEEG in preterm brain damage

Acute

• Acute brain injury (IVH/PVL) associated with depressed background activity, lack of SWC and seizures

• aEEG/EEG depression correlates with severity of IVH grade

Chronic

• Delayed or abnormal EEG maturation, and abnormal wave forms
The Maximum number of Bursts/h predicted outcome in preterm infants with IVH 3-4

(Hellström-Westas et al, Neuropediatrics 2001)

Table 2 Maximum and minimum bursts/hour during the first week of life in 64 preterm (28 survivors and 36 non-survivors) infants with IVH grade III – IV, mean (SD)

<table>
<thead>
<tr>
<th>Postnatal hours</th>
<th>aEEG recordings (n)</th>
<th>Maximum Bursts/h survivors</th>
<th>Maximum Bursts/h non-survivors</th>
<th>p value</th>
<th>Minimum Bursts/h survivors</th>
<th>Minimum Bursts/h non-survivors</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 24</td>
<td>32</td>
<td>130 (36)</td>
<td>99 (41)</td>
<td>0.033</td>
<td>81 (34)</td>
<td>58 (35)</td>
<td>NS</td>
</tr>
<tr>
<td>24 – 48</td>
<td>41</td>
<td>137 (31)</td>
<td>109 (36)</td>
<td>0.011</td>
<td>78 (37)</td>
<td>55 (40)</td>
<td>NS</td>
</tr>
<tr>
<td>48 – 72</td>
<td>40</td>
<td>141 (29)</td>
<td>119 (39)</td>
<td>0.049</td>
<td>75 (45)</td>
<td>55 (36)</td>
<td>NS</td>
</tr>
<tr>
<td>72 – 96</td>
<td>32</td>
<td>132 (38)</td>
<td>105 (31)</td>
<td>0.032</td>
<td>79 (44)</td>
<td>63 (45)</td>
<td>NS</td>
</tr>
<tr>
<td>96 – 120</td>
<td>24</td>
<td>134 (28)</td>
<td>112 (40)</td>
<td>NS</td>
<td>89 (42)</td>
<td>63 (51)</td>
<td>NS</td>
</tr>
<tr>
<td>120 – 144</td>
<td>19</td>
<td>133 (34)</td>
<td>116 (26)</td>
<td>NS</td>
<td>74 (48)</td>
<td>79 (30)</td>
<td>NS</td>
</tr>
<tr>
<td>144 – 168</td>
<td>12</td>
<td>130 (44)</td>
<td>130 (22)</td>
<td>NS</td>
<td>88 (42)</td>
<td>95 (38)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Poor outcome (death/severe NDI) correctly predicted in 78% at 24-48 h by MaxBurst <130/h
Early aEEG predicts outcome in very preterm infants *(Song et al Sci Rep 2015)*

- N=324 very preterm infants (mean GA 30 w):
  - At 18 months: 262 good / 62 poor outcome
- White matter damage (WMD) on MRI strongly associated with aEEG lower border amplitude and cyclicity <72hrs
- CP and poor outcome (death, CP, NDI) best predicted by aEEG + MRI (PPV/NPV 77/98% and 79/77%, respectively)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>aEEG (n = 139)</td>
<td>83.3</td>
<td>58.2</td>
<td>15.9</td>
<td>97.4</td>
<td>75.0</td>
<td>60.9</td>
<td>28.6</td>
<td>92.1</td>
</tr>
<tr>
<td>HUS (n = 308)</td>
<td>87.5</td>
<td>64.5</td>
<td>11.9</td>
<td>98.9</td>
<td>65.2</td>
<td>66.4</td>
<td>25.4</td>
<td>89.7</td>
</tr>
<tr>
<td>MRI (n = 210)</td>
<td>68.8</td>
<td>90.2</td>
<td>36.7</td>
<td>97.2</td>
<td>50.0</td>
<td>92.1</td>
<td>53.3</td>
<td>91.1</td>
</tr>
<tr>
<td>aEEG + HUS (n = 139)</td>
<td>83.3</td>
<td>78.7</td>
<td>27.0</td>
<td>98.0</td>
<td>66.7</td>
<td>79.1</td>
<td>40.0</td>
<td>91.9</td>
</tr>
<tr>
<td>aEEG + MRI (n = 100)</td>
<td>83.3</td>
<td>96.6</td>
<td>76.9</td>
<td>97.7</td>
<td>52.4</td>
<td>96.2</td>
<td>78.6</td>
<td>88.4</td>
</tr>
<tr>
<td>HUS + MRI (n = 209)</td>
<td>68.8</td>
<td>93.8</td>
<td>47.8</td>
<td>97.3</td>
<td>45.2</td>
<td>93.8</td>
<td>56.0</td>
<td>90.8</td>
</tr>
<tr>
<td>aEEG + HUS + MRI (n = 100)</td>
<td>83.3</td>
<td>96.6</td>
<td>76.9</td>
<td>97.7</td>
<td>52.4</td>
<td>96.2</td>
<td>78.6</td>
<td>88.4</td>
</tr>
</tbody>
</table>
Multiple logistic regression: GA and IVH/PVL did not predict outcome.

aEEG:
- BS >2 h: sens/spec/PPV/NPV/correctly predicted: 89/64/68/88/76%
- EEG (at 24h): >50% suppressed: sens/spec/PPV/NPV/correctly predicted: 72/82/76/78/78%

EEG - but not GA or IVH/PVL - predicted outcome (multiple logistic regression): EEG >50% suppressed at 24 h:
- Sens/spec/PPV/NPV: 72/82/76/78%
- Correctly predicted: 78%

BS duration >2 h first 72 h:
- sens/spec/PPV/NPV/corr: 89/64/68/88%
- Correctly predicted: 76%

Median scores: *
Cyclicity "sleep wake cycling" in very preterm infants

Middel et al, Neonatology 2018:
• N=41, GA 26-32.9 w, assessed at 7.39 years.
• Cyclicity directly after birth associated with higher total IQ (104 vs 97, p=0.05) and higher visual perception scores.
• Depressed aEEG not associated with poorer outcomes.

(Wikström et al, Acta Paediatr 2012)
Acute and Chronic responses to cerebral recorded by aEEG

Acute
Chronic
Acute and Chronic
responses to cerebral
recorded by aEEG
Chronic-stage EEG abnormalities in preterm infants (Okumura et al, Dev Med Child Neurol 2002)

N= 183 infants, GA<33w and BW<2000g. EEG: <72 h, and repeated weekly until term. Cerebral ultrasound (IVH/PVL). Follow up 18 months.

Chronic stage abnormalities (n=80/183, 44%):

• **Disorganized** (abnormal wave forms/organization):
  n=52 (31 had PVL and 7 IVH)
  CP (n=39, 75%), normal cognition (n=26, 50%)

• **Dysmature** (delayed):
  n=28 (1 had PVL and 11 IVH)
  CP (n=5, 18%), subnormal cognition (n=20, 71%)
Marret et al: N=301, prospective study
- no PRSW (98.2%) = favorable motor outcome
- PRSW: sensitivity 98%/specificity 84% developmental motor disability; 96% sensitivity severe spastic diplegia.
- >2 PRSW per minute specific sign of severe spastic diplegia

Okumura et al: N=93 (31 PVL/62 control), retrospective study
- PRSW only present in infants with PVL, always part of disorganized EEG
- PRSW associated with moderate/severe diplegia
Prognostic value of conventional EEG in preterm infants \cite{hayashi-kurahashi-etal-2012} 

N = 333 infants GA < 34 w, 780 EEGs, at 12-18 months cerebral palsy (CP) in 34 and developmental delay (DD) in 33.

EEG abnormalities (<37 days) predictive of DD and CP but only during period 2 (day 7-19) independent predictor of DD, OR 3.2 (95%CI 1.1-9.7) and CP, OR 6.8 (95%CI 2-23) (controlling for clinical variables and severe brain injury)

\begin{table}
\centering
\begin{tabular}{|l|c|c|c|c|}
\hline
 & Developmental Delay and/or Cerebral Palsy & & & \\
 & Sensitivity & Specificity & PPV & NPV \\
\hline
\hline
Any grade of EEG abnormality & & & & \\
First period & 0.61 (0.45–0.75) & 0.74 (0.68–0.80) & 0.27 (0.19–0.38) & 0.92 (0.88–0.95) \\
Second period & 0.60 (0.44–0.74) & 0.84 (0.79–0.88) & 0.36 (0.25–0.49) & 0.93 (0.89–0.96) \\
Third period & 0.50 (0.35–0.66) & 0.86 (0.80–0.90) & 0.38 (0.26–0.53) & 0.91 (0.86–0.94) \\
\hline
Moderate to severe grade of EEG abnormality & & & & \\
First period & 0.41 (0.27–0.58) & 0.92 (0.88–0.95) & 0.46 (0.30–0.62) & 0.91 (0.87–0.94) \\
Second period & 0.27 (0.15–0.43) & 0.95 (0.92–0.97) & 0.48 (0.28–0.68) & 0.90 (0.85–0.93) \\
Third period & 0.25 (0.14–0.41) & 0.96 (0.92–0.98) & 0.50 (0.29–0.71) & 0.88 (0.83–0.91) \\
\hline
\end{tabular}
\end{table}
Neonatal EEG and neurodevelopmental outcome in preterm infants born before 32 weeks

Maximilien Périvier, Jean-Christophe Rozé, Géraldine Gascoin, Matthieu Hanf, Bernard Branger, Valérie Rouger, Isabelle Berlie, Yannis Montcho, Yann Péron, Cyril Flamant, Sylvie Nguyen The Tich

2040 eligible infants with a gestational age of less than 32 weeks
1954 infants enrolled in LIFT cohort
20 had genetic syndromes and/or death after discharge
190 were not assessed at 2 years of age
1744 children assessed at 2 years of age, including 1345 with at least one EEG
422 had non-optimal neurodevelopment
1322 had optimal neurodevelopment

Table 2  EEG surveillance abnormalities as a risk factor for global neurodevelopment at 2 years of corrected age analysis

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>OR</th>
<th>95% CI</th>
<th>p Value</th>
<th>aOR*</th>
<th>95% CI</th>
<th>p Value</th>
<th>aOR†</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (Grade 0)</td>
<td>976</td>
<td>1</td>
<td>0.79 to 1.40</td>
<td>0.75</td>
<td>1.11</td>
<td>0.83 to 1.48</td>
<td>0.49</td>
<td>1.06</td>
<td>0.78 to 1.42</td>
<td>0.75</td>
</tr>
<tr>
<td>EEG not performed</td>
<td>399</td>
<td>1.05</td>
<td>0.79 to 1.40</td>
<td>0.75</td>
<td>1.11</td>
<td>0.83 to 1.48</td>
<td>0.49</td>
<td>1.06</td>
<td>0.78 to 1.42</td>
<td>0.75</td>
</tr>
<tr>
<td>Transient moderate</td>
<td>269</td>
<td>1.88</td>
<td>1.39 to 2.53</td>
<td>0.001</td>
<td>1.72</td>
<td>1.27 to 2.33</td>
<td>0.001</td>
<td>1.49</td>
<td>1.08 to 2.04</td>
<td>0.01</td>
</tr>
<tr>
<td>EEG surveillance</td>
<td>100</td>
<td>4.43</td>
<td>2.90 to 6.76</td>
<td>0.001</td>
<td>4.12</td>
<td>2.68 to 6.34</td>
<td>0.001</td>
<td>2.38</td>
<td>1.49 to 3.81</td>
<td>0.001</td>
</tr>
<tr>
<td>Very abnormal EEG</td>
<td>100</td>
<td>4.43</td>
<td>2.90 to 6.76</td>
<td>0.001</td>
<td>4.12</td>
<td>2.68 to 6.34</td>
<td>0.001</td>
<td>2.38</td>
<td>1.49 to 3.81</td>
<td>0.001</td>
</tr>
<tr>
<td>EEG surveillance (Grade 2, detailed):</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Permanent moderate</td>
<td>67</td>
<td>3.00</td>
<td>1.80 to 4.98</td>
<td>0.001</td>
<td>2.67</td>
<td>1.59 to 4.48</td>
<td>0.001</td>
<td>1.62</td>
<td>0.92 to 2.87</td>
<td>1</td>
</tr>
<tr>
<td>Transient severe</td>
<td>24</td>
<td>7.86</td>
<td>3.32 to 18.6</td>
<td>0.001</td>
<td>7.48</td>
<td>3.11 to 17.99</td>
<td>0.001</td>
<td>4.43</td>
<td>1.77 to 11.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Permanent severe</td>
<td>9</td>
<td>31.4</td>
<td>3.91 to 252</td>
<td>0.001</td>
<td>36.82</td>
<td>4.52 to 299.8</td>
<td>0.001</td>
<td>12.45</td>
<td>1.43 to 108.1</td>
<td>0.02</td>
</tr>
</tbody>
</table>

*Adjustment for gestational age, birth weight Z-score and sex.
†Adjustment for gestational age, birth weight Z-score, sex, neurological assessment at discharge and cerebral lesions in neonatal imaging.
Term-equivalent functional brain maturational measures predict neurodevelopmental outcomes in premature infants

Nathalie M. El Ters, Zachary A. Vesoulis, Steve M. Liao, Christopher D. Smyser, Amit M. Mathur

- N=44, GA 26(2)w, PMA at study 39(2)w, aEEG/SEF\textsubscript{90}, MRI
  - IVH 3-4 (43.2%); surgery: NEC (15.9%), PDA (13.6%); ROP (29.5%); postnatal steroids (34.1%); oxygen at 36 w (77.3%);
  - Moderate/severe injury on MRI at term equivalent age (56.8%)
  - At 24-36 months: motor delay (61%) language delay (52%), cognitive delay (54%)

<table>
<thead>
<tr>
<th>aEEG measures at TEA and developmental delay at 24–36 months corrected age.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No motor delay</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Left SEF\textsubscript{90}</td>
</tr>
<tr>
<td>Right SEF\textsubscript{90}</td>
</tr>
<tr>
<td>Absent cyclicity</td>
</tr>
</tbody>
</table>

Odds ratio of developmental delay associated with SEF\textsubscript{90} and absent cyclicity.

<table>
<thead>
<tr>
<th>Motor delay</th>
<th>Language delay</th>
<th>Cognitive delay</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR (95% CI), p-value</td>
<td>OR (95% CI), p-value</td>
<td>OR (95% CI), p-value</td>
</tr>
<tr>
<td>----------------</td>
<td>----------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Left SEF\textsubscript{90} &lt; 9.2</td>
<td>4.7 (1.2–18.3), p = 0.02*</td>
<td>3.0 (0.8–10.7), p = 0.09</td>
</tr>
<tr>
<td>Right SEF\textsubscript{90} &lt; 9.2</td>
<td>7.9 (1.8–34.5), p &lt; 0.01*</td>
<td>5.9 (1.5–23.1), p = 0.01*</td>
</tr>
<tr>
<td>Absent cyclicity</td>
<td>5.8 (1.3–25.1), p = 0.01*</td>
<td>1.6 (0.4–5.7), p = 0.4</td>
</tr>
<tr>
<td>Absent cyclicity + SEF\textsubscript{90} &lt; 9.2</td>
<td>19.2 (3.9–94.1), p &lt; 0.01*</td>
<td>12.0 (2.2–65.5), p &lt; 0.01*</td>
</tr>
</tbody>
</table>
Spectral edge frequency and white matter injury

(Inder et al, Pediatrics 2003)
Burst shapes and outcome in extremely preterm infants (Iyer et al, Brain 2015 and Crit Care med 2015)

- Single-ch EEG from 43 extremely preterm infants
- 90-120 min relative artefact free epochs at 12-24-48-72 hrs
- Development of IVH associated with increased sharpness (kurtosis)
- Burst shape (slope) at 12 h predicted 2-year MDI
- Kurtosis and symmetry at 72 h predicted 2-year MDI and PDI
Conclusion: Prediction of outcome with aEEG and EEG in term and preterm infants

- aEEG and EEG give direct information about brain function in both term and preterm infants, which can be used for predicting gross outcome, both in the acute and chronic stages of illness.

- Such predictions can be used for guiding medical investigations and interventions/treatment, and for informing parents.

- The main aEEG and EEG features used for evaluation include:
  - Acute changes: Background activity, cyclicity, seizures
  - Chronic changes: Organization and maturation, sleep, abnormal waveforms (PRSW, e.g. delta brushes), als SEF (spectral edge frequency) seems to be a promising measure.
Acknowledgements

• Linda de Vries (Utrecht, the Netherlands)
• Sampsa Vanhatalo (Helsinki, Finland)
• Gorm Greisen (Copenhagen, Denmark)
• Marianne Thoresen (Oslo, Norway)
• Ingmar Rosén, Nils Svenningsen†, Sverre Wikström, David Ley (Lund, Sweden)
• Kartik Iyer, James Roberts, Michael Breakspear (Brisbane, Australia)