Early development of the EEG activity: 
Function vs. Structure

Sampsa Vanhatalo, MD PhD
Dept.Clin.Neurophys, Children’s Hospital
Univ. Hospital of Helsinki, Finland

Wien 2008

Is preterm & neonatal EEG difficult?

Yes
Well...yes
No...LIARS?
No!

Two approaches

Phenomenology
(phenography)

Physiology

Two approaches

Phenomenology
Long & good clinical tradition: read the graphoelements
mostly based on the work by French pioneers

Currently the basis for ALL clinical neonatal EEG
Perplexing to many.
No physiology in it.

Hence easier alternatives expanding (aEEG/CFM)
Perplexity: Terms & Concepts

**EEG terms (e.g.):**
- Delta waves at 0.3-2 Hz
- Delta-brush
- Delta crest
- Spindle-shaped bursts of fast activity
- Rapid rhythm
- Rapid bursts
- Spindle-like fast
- Fast activity at 14-24 Hz
- Ripples of prematurity
- Positive slow wave

**What?**
EEG events with simultaneous slow & fast activity, but different
- authors
- recording device
- brain area?
- conceptional age?

Nature may be tricky, but is there a biological approach?

Physiology

Relation between brain & signal (EEG)?

1. What happens & where?
2. Why?
3. So what?

Translational studies

<table>
<thead>
<tr>
<th>Human</th>
<th>Animal models</th>
</tr>
</thead>
</table>

A challenging way, but the current medicine gives no options

Developing macrostructure

Ivica Kostovic et al.

Developing long connections (& subplate)

-23 wks
24-32 wks
32+ wks
Developing microstructure

<table>
<thead>
<tr>
<th>Preterm</th>
<th>Postterm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Th-Cx axons</td>
<td>Intracortical, short-range</td>
</tr>
</tbody>
</table>

Structural milestones re function

**Preterm:**
- Subplate
- Thalamo-cortical connections
- Cortico-cortical connections
  - Corpus callosum (interhemispheric)
  - Postero-anterior connections (intrahemispheric)

**Post-term**
- Cortico-cortical connections (local)

Transience & coexistence

1. transient structures ➔ transient functions
2. prolonged coexistence
   1. subplate-cortex
   2. corpus callosum

How?

Cortex has $27 \times 10^9$ neurons
Brain has $75 \times 10^9$ neurons
> 10-50 000/s born!
Each one has thousands of synapses!
Most distant ones are eons away!

- Numbers and distances are astronomical!
- Genes can not directly govern this!
- An epigenetic mechanism is required!
The major challenge is to find the correct friends 😊

"Fire together and wire together"

 совершаем связь вместе. How to fire together?

- Only one mechanism can help in telling friends apart from aliens
- SHOUT and connect with the other noisy ones!

Brain also:
EVERY place in the early brain shows spontaneous, intermittent activity.

Early vs. late activity

Spontaneous activity in brain stem and spinal cord

Momose-Sato et al, 2007
The Michigan-electrode

\[125 \mu m - 150 \mu m\]

Nature Neuroscience, 2005

Vanhatalo & Lauronen, SFNM, 2006

(A.Hrbek/Göteborg/humans and Meyerson/Karolinska/sheep, 1960-70s)

Why do we see it in ALL other animals, but reported in humans?

1) It is not there? ABSURD!

2) It is there, but we do not recognize it? YES!

Missing? Translational research (comparison to exp. work) abandoned in the early 1970s plus…
Yet the literature…:
major features in the early EEG are "bursts of slow activity" and discontinuity (read: not much between these bursts!)

Spontaneous Activity Transients (SAT)

SATs are moving!

26 wks

Early preterm (28 wks)
Moderately preterm (29-33 wks)
Fullterm (38+ wks)
**Two-Component Framework**

Vanhatalo & Kaila, Seminars in Fetal and Neonatal Medicine, 2006

**Structure vs. age vs. function**

<table>
<thead>
<tr>
<th>Structure</th>
<th>time</th>
<th>EEG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Only local columnar</td>
<td>until early preterm</td>
<td>none or focal only intermittent (SAT)</td>
</tr>
<tr>
<td>Th-cx connections</td>
<td>25-32</td>
<td>wider extent (SAT) also continuous (Ongoing)</td>
</tr>
<tr>
<td>Callosal connections</td>
<td>34+</td>
<td>Interhemispheric coordination (SAT) fully continuous, (Ongoing)</td>
</tr>
<tr>
<td>Long cx – cx connections</td>
<td>34+</td>
<td>Intrahemispheric coordination (SAT) (long-range) (Ongoing)</td>
</tr>
<tr>
<td>Short cx-cx</td>
<td>late preterm – post term</td>
<td>faster rhythmic activity (ongoing)</td>
</tr>
</tbody>
</table>

**Th-cx growth vs. sensory input??**

Vanhatalo & Lauronen, SFNM, 2006

(A.Hrbek/Göteborg/humans and Meyerson/Karolinska/sheep, , 1960-70s)

**Practice?**

somatosensory pathway
So What?

Function needs the Structure & Structure needs the Function

Cortical activity (SATs) vs. CO₂ or anesthesia?

Neonate brains are extremely sensitive especially to our care!

Th-cx connections vs. activity (by sensory input)

Spontaneous activity vs. neuronal survival

Optimal for *BDNF-secretion & cAMP cascade

Remember the gray matter loss in the MRI!!!
"Please say it in aEEG language!"

Burst level (SAT detector) – a novel "brain trend"? (ala satO₂)

many bursts => good baby
few bursts => bad baby

(Hellström-Westas et al, NeoReviews, 2006)

Technical development?

All sufficient technology is there: recording, stimulation, analysis.
However, not provided by the most massive companies!

There are two ways to approach the brain:

1. Choose the tool => your target (=signal) is what the tool hits.
2. Choose the target => your tool will need to see your target.

Electrode number? Anything is feasible!
Take home:

Lege artis neonatal EEG…

1) Is badly needing mechanistic understanding
2) Synchronization and amount matter in the development
3) Choose the tools wisely to see right things!
4) New views opening to see what really matters
5) Chances opening to perform real translational studies bidirectional!