Rett syndrome

Unmasking complex cardio-respiratory dysfunction and possible treatment.

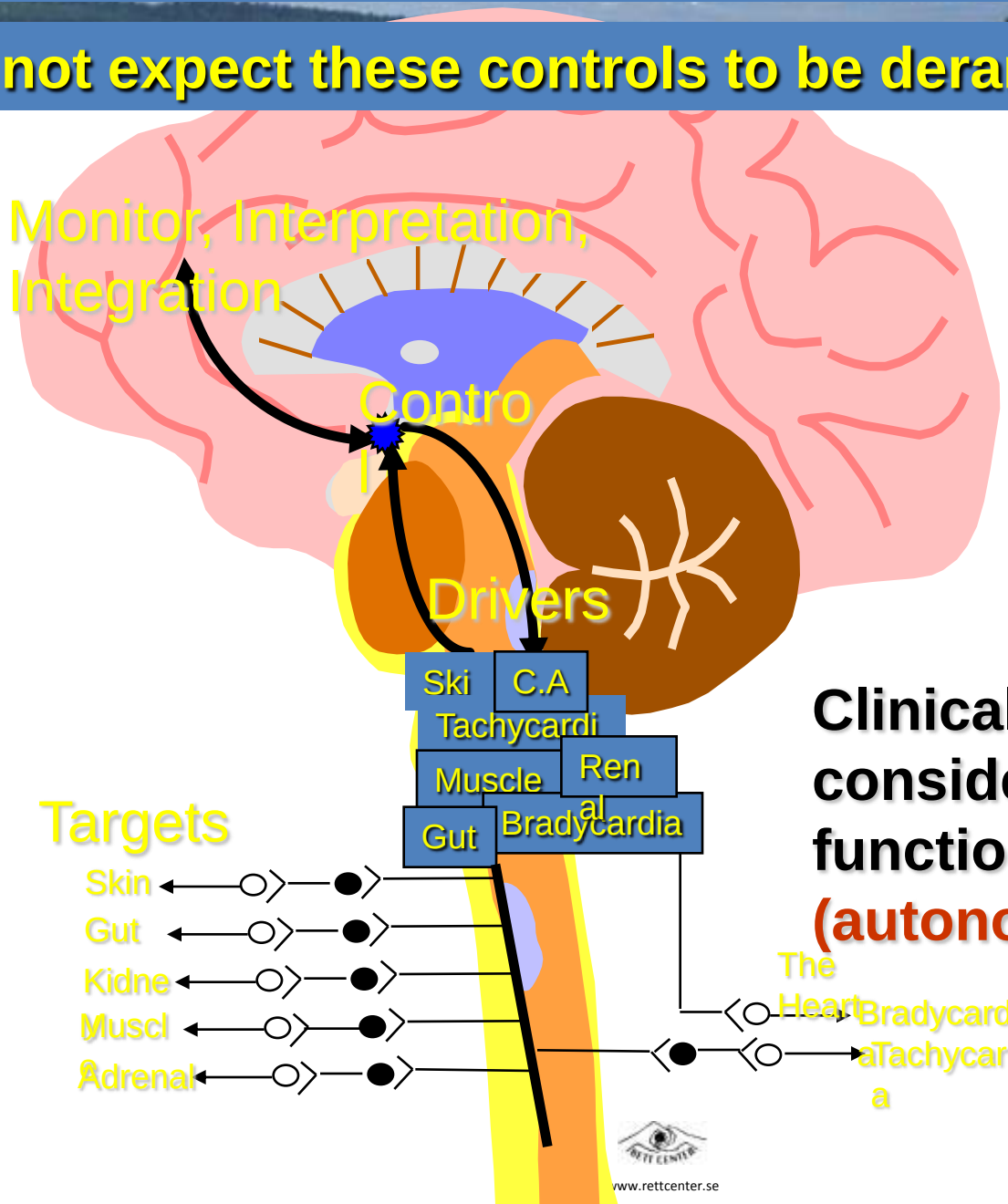
Ingegerd Witt Engerström
MD. PhD. Paediatric neurologist
Medical Director, Swedish Rett Center
www.rettcenter.se

RETT SYNDROME

- Rare
  (1:10.000 girls)
- Genetic – seldom inherited
  (> 99% sporadic)
- Neuro-developmental disorder – not progressive!
- Immature brainstem/brain
- Central control of the autonomic nervous system insufficient/deranged
- Breathing dysrhythmia
- Blood pressure & heart rate uncontrolled
- Blood circulation in tissues deranged
- Agitation and seizures
- Epilepsy
- Gastrointestinal dysfunction
- Incoordination of thoughts and movements

We are dealing with basic human physiology

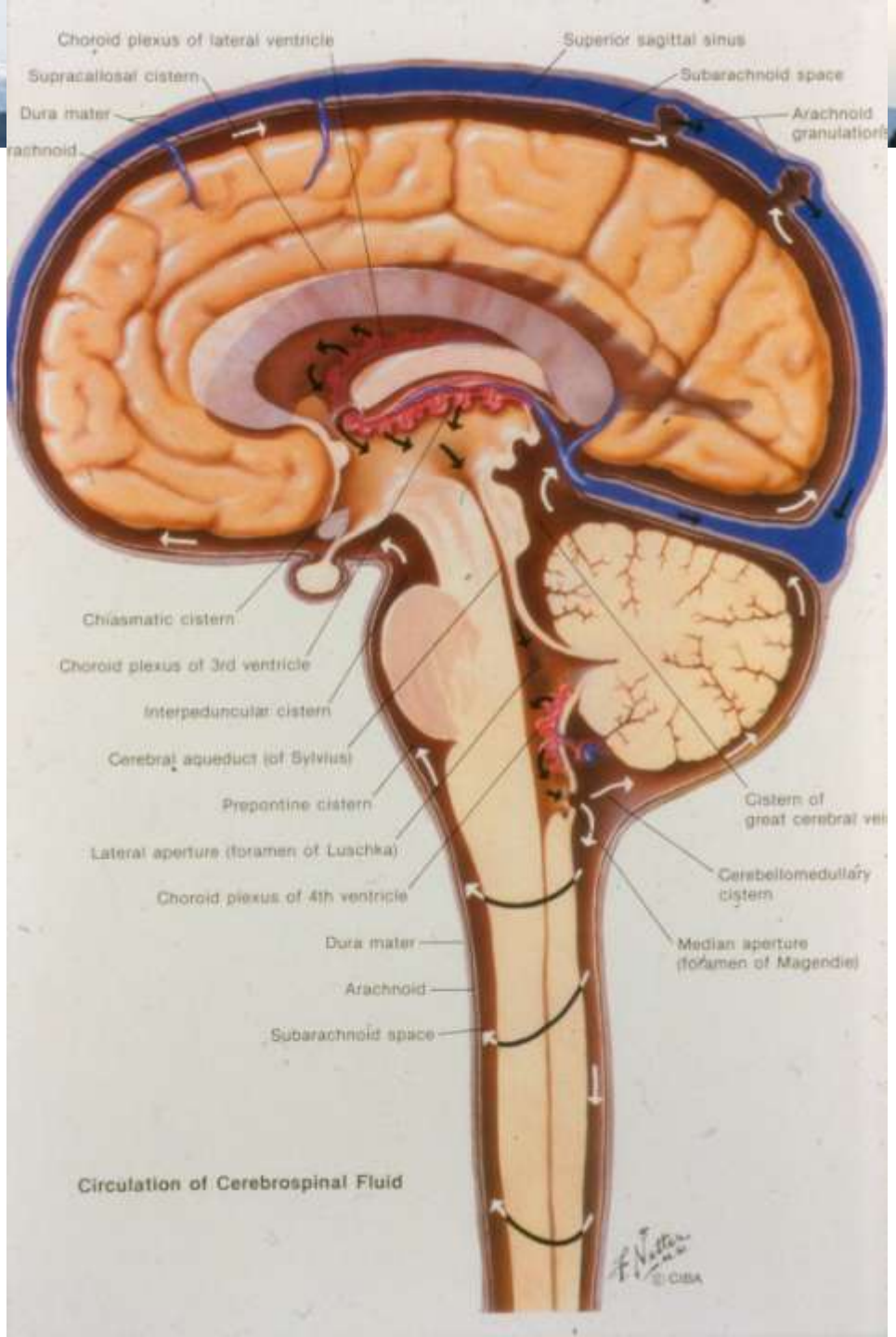
We do not expect these controls to be deranged



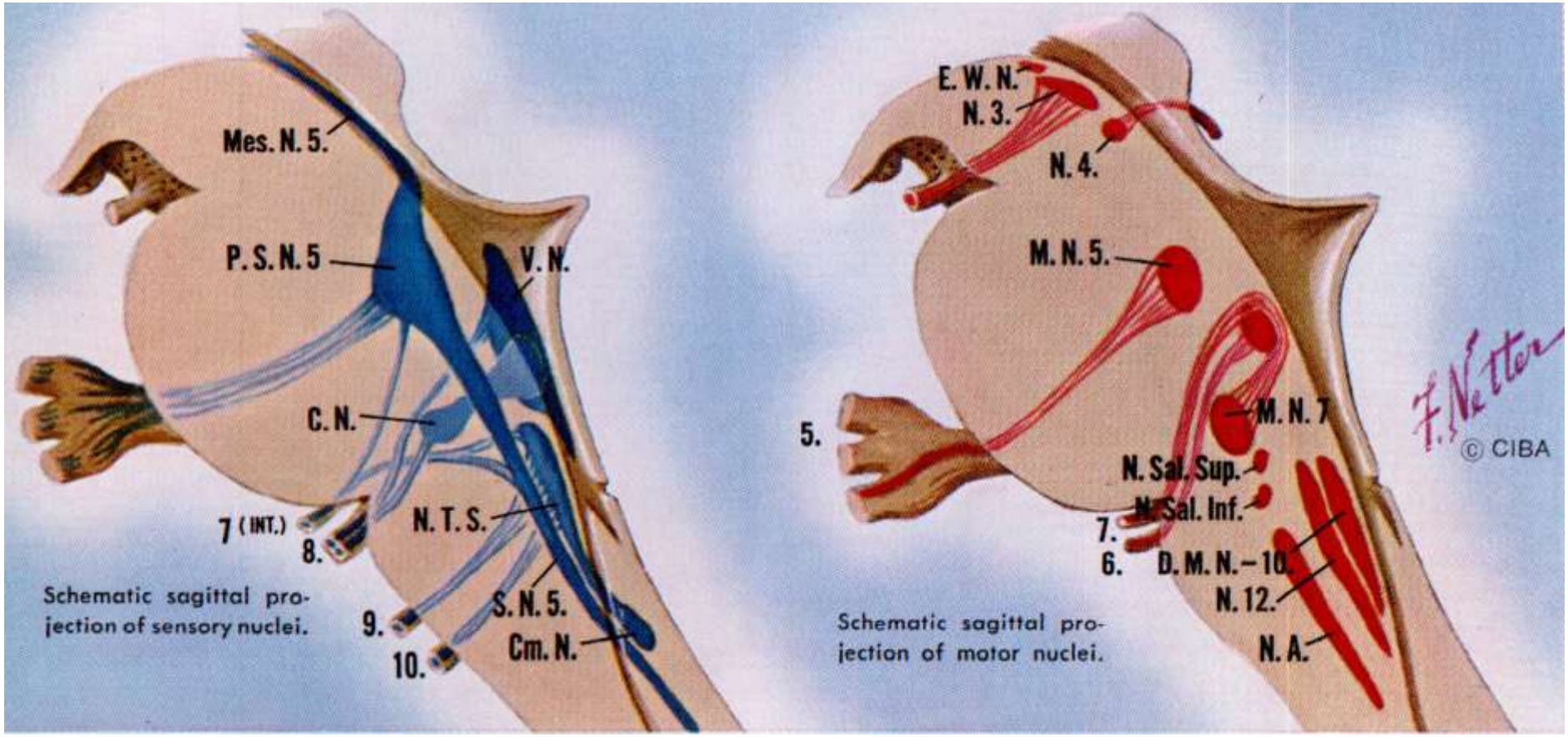
Clinical exams must consider these functional units (autonomic nuclei)

Brainstem features

- Breathing dysrhythmia, insufficient control of blood gases, unstable blood pressure and heart rate.
- Oropharyngeal and gastrointestinal dysfunctions cause swallowing difficulties, aspiration, gastrooesophageal reflux, oesophagitis and constipation.
- Agitation, fear, mood swings, difficulty to relax and concentrate, cold and discoloured feet.
- Extrapyramidal symptom: dystonia with orthopaedic deformities, muscle wasting, incoordination of thoughts and movements.


Choroid plexus of lateral ventricle
Superior sagittal sinus
Supracallosal cistern
Subarachnoid space
Dura mater
Arachnoid granulation
Chiasmatic cistern
Choroid plexus of 3rd ventricle
Interpeduncular cistern
Cerebral aqueduct (of Sylvius)
Prepontine cistern
Cistern of great cerebral vei
Lateral aperture (foramen of Luschka)
Cerebellomedullary cistern
Choroid plexus of 4th ventricle
Dura mater
Median aperture (foramen of Magendie)
Arachnoid
Subarachnoid space
Circulation of Cerebrospinal Fluid
© CIBA

Organisation of brainstem nuclei in adults



Sensory

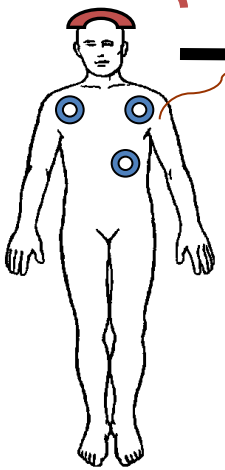
Motor

We require Cortico-Bulbar Neurophysiology

EEG

Video

Subject

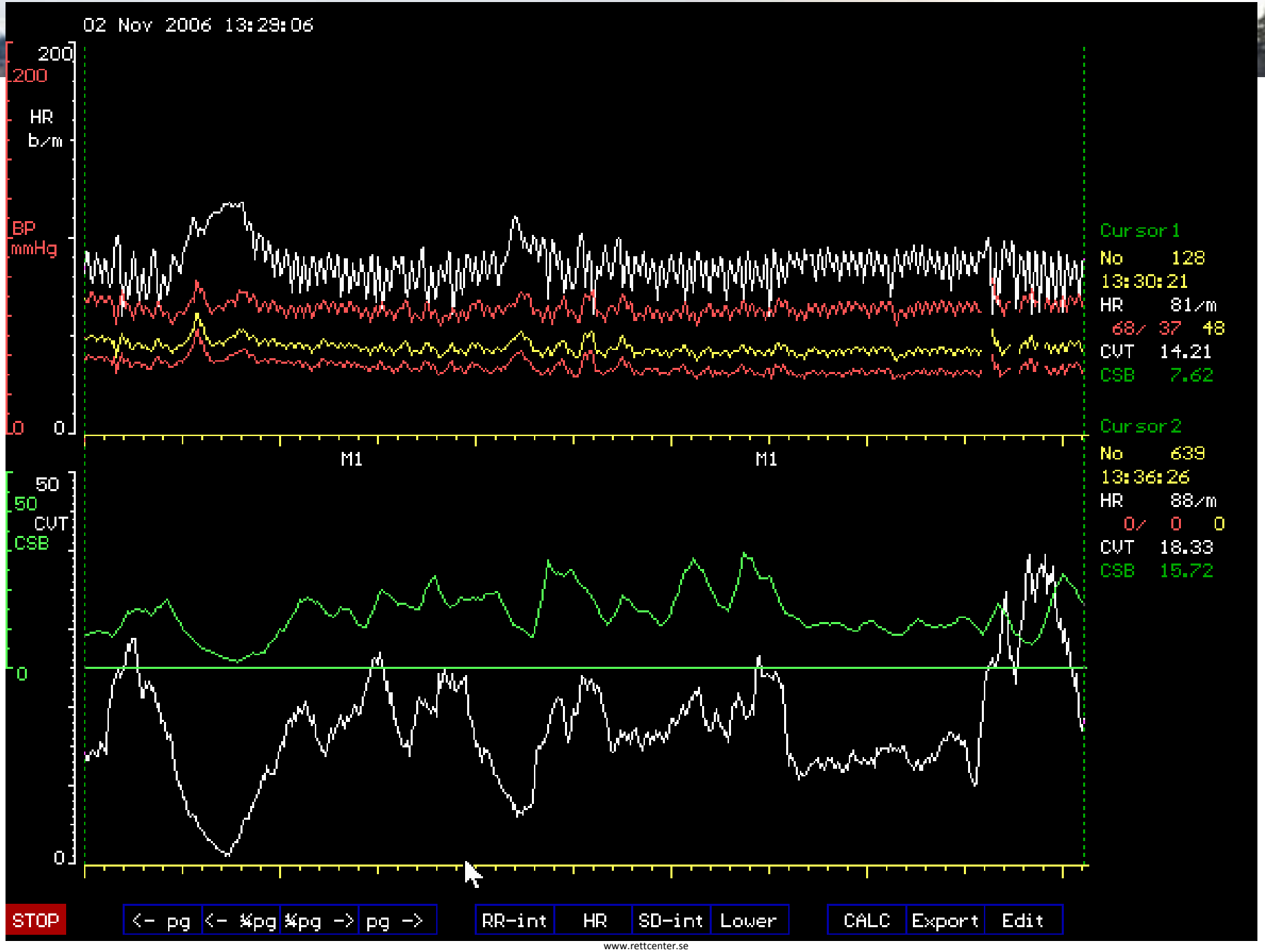


NeuroScope

Beat-to-beat non-invasive BP

Breathing movement

Transcutaneous pO_2 and pCO_2



The Frösö Declaration

Addressing the cardiorespiratory challenges posed by Rett Syndrome in Medicine.

Peter O O Julu, Ingegerd Witt Engerström, Stig Hansen, Flora Apartopoulos, Bengt Engerström, Giorgio Pini, Robert S Delamont, Eric EJ Smeets.

The Lancet 200;371:1981-83.

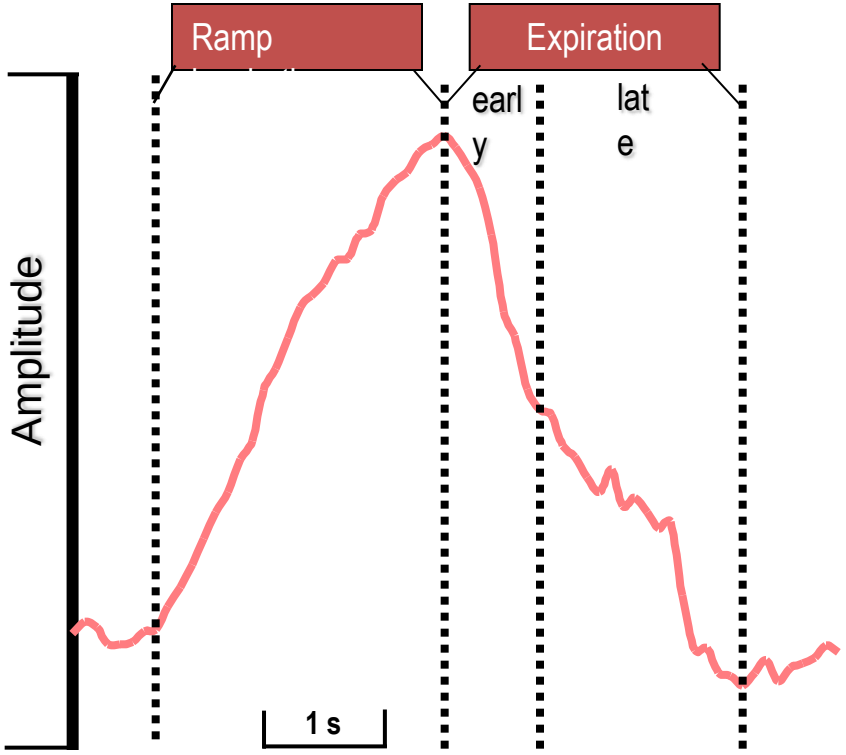
Three cardiorespiratory phenotypes

- Forceful breathers
- Feeble breathers
- Apneustic breathers

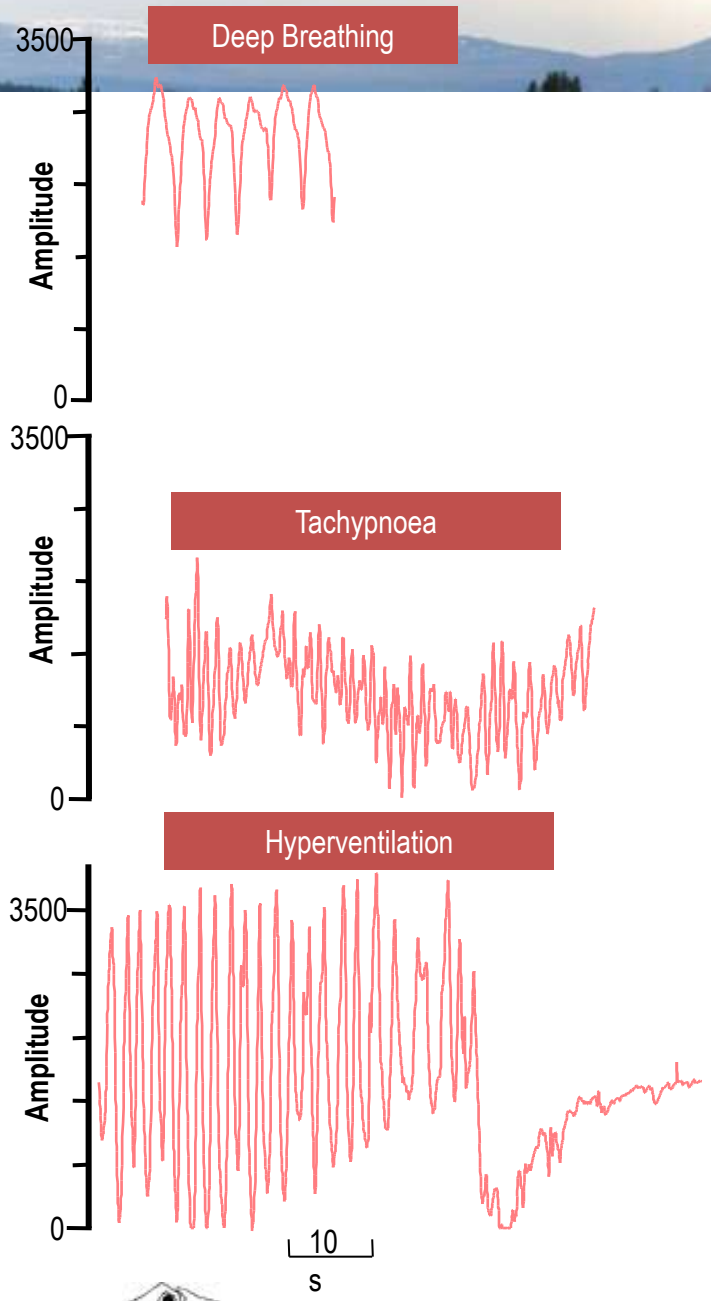
Three cardiorespiratory phenotypes

- Nutritional needs can be doubled the normal value for forceful breathers.
- Feeble or apneustic breathers may not restart spontaneous breathing post-operatively due to artificial hyperventilation.
- Feeble breathers are sensitive to sedation (Opioids and Diazepam) and these drugs can cause apnoea.
- Valsalva's manouver is a common complication in Rett syndrome.

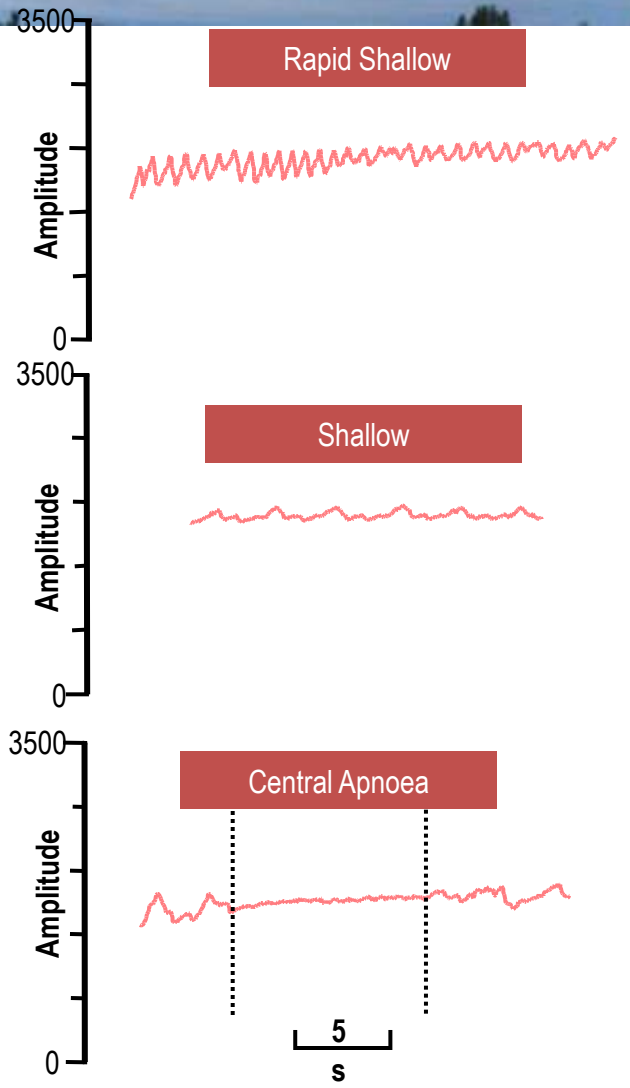
Measurement of breathing movements :



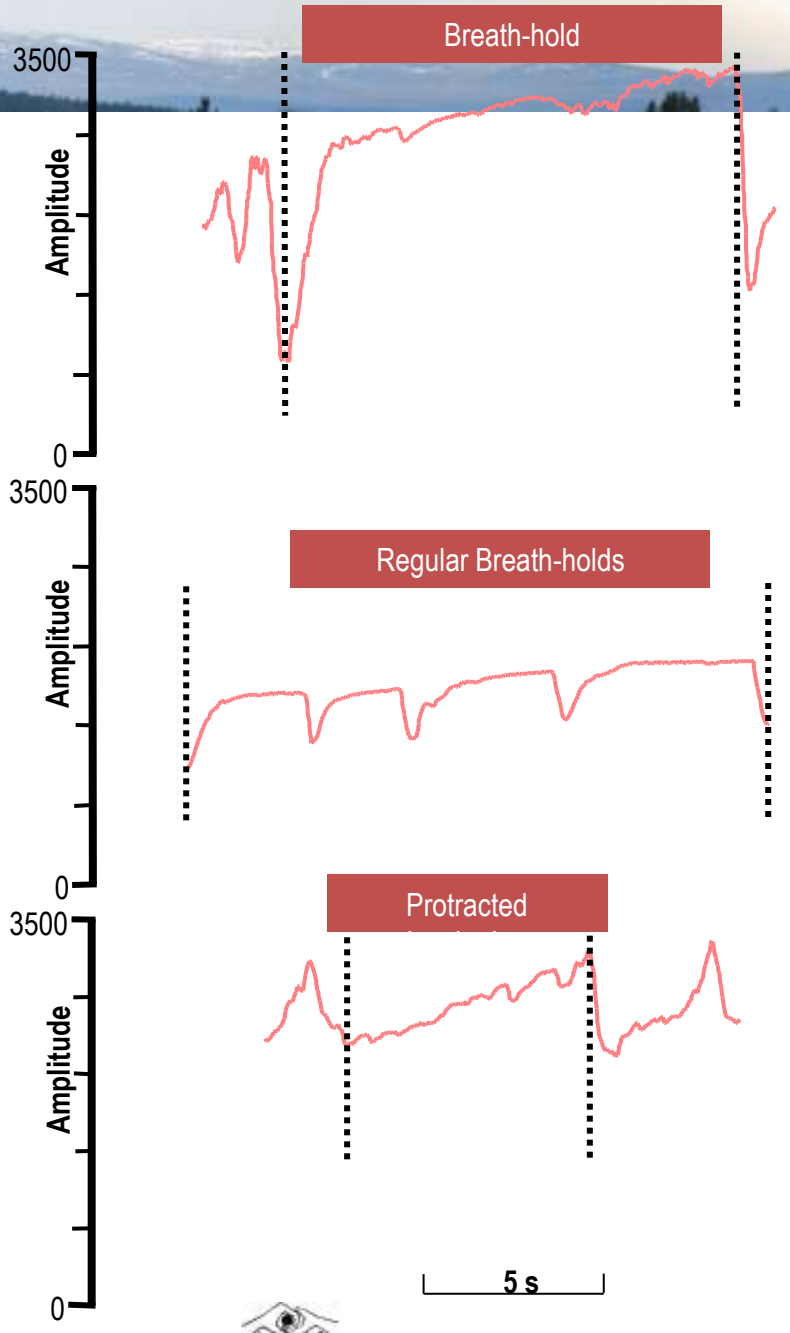
Forceful Breathing



Feeble Breathing



Apneustic Breathing



Valsalva manoevre in girl with Rett syndrome

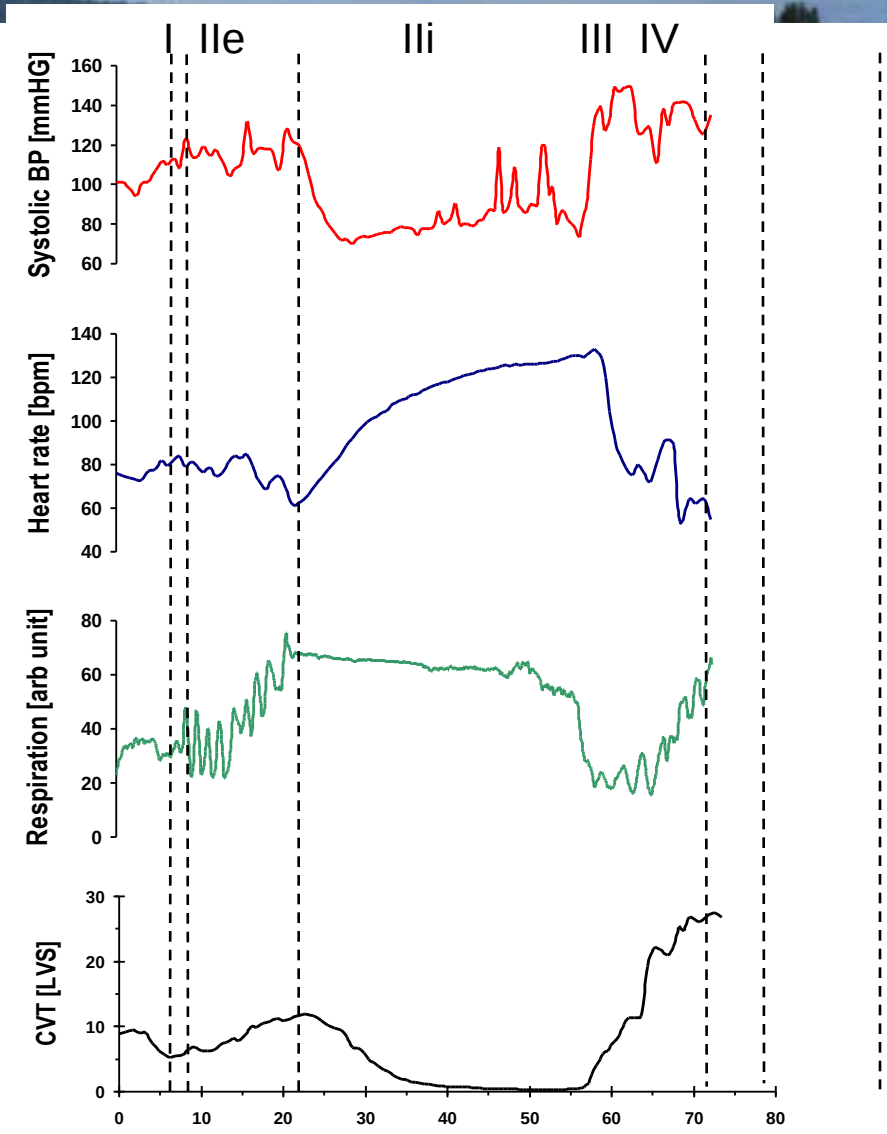


Figure 2

Some movement artefacts are present

Treatment of breathing dysfunction in Rett syndrome

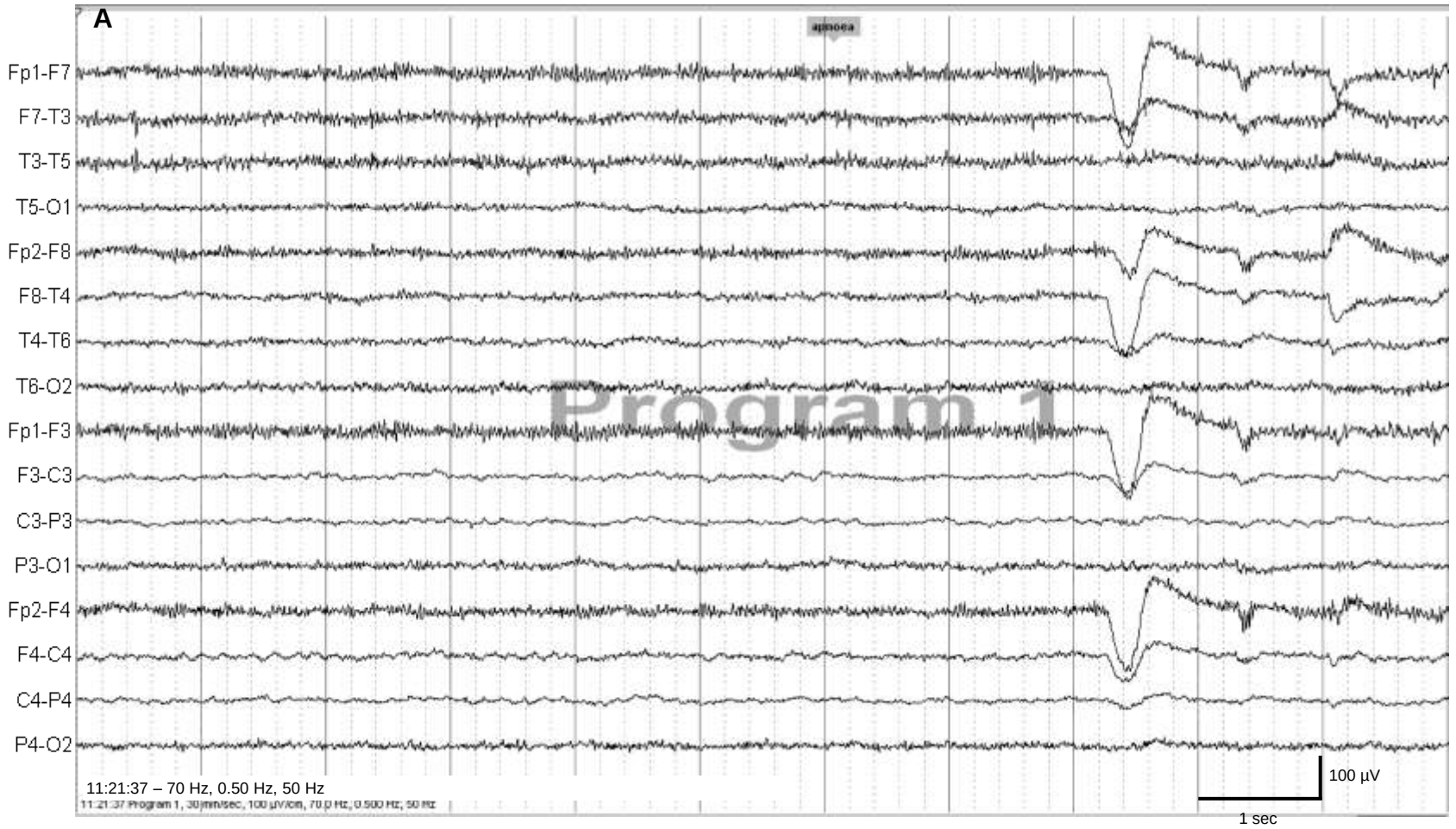
- **Forceful breathers**: Rebreathing of own expired air in a rebreathing mask with adjusted dead space, when awake.
- **Feeble breathers**: Assisted breathing with CPAP or Bi-PAP, mainly at night. Sometimes using an oxygen concentrator initially.
- **Apneustic breathers**: Buspirone to shorten apneustic breaths, if not too much feeble breathing.

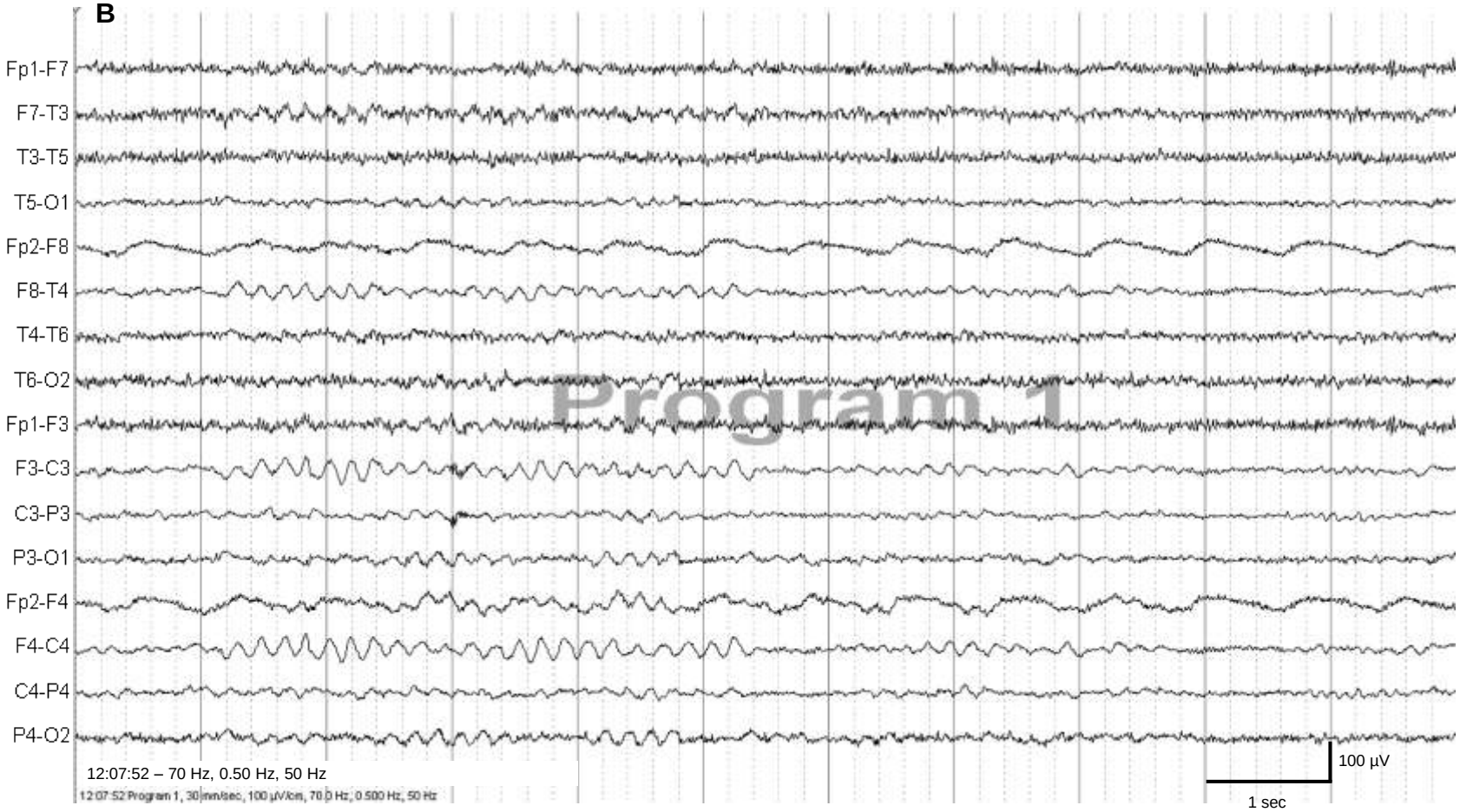
Outcome of treatment of a forceful breather with Rett syndrome with a rebreathing mask.

- Increased attentiveness and interest at home and in school.
- Face expressive and smiling in stead of mimicless and serious.
- Muscles less tense, more relaxed.
- Increased muscle strength being able to stand up longer.
- Dramatic decrease of seizures.
- Decrease of cyanosis from several times each day to once in 4 months.
- Normal colour of lips and face.
- Normalisation of colour and temperature of feet (earlier cold and bluish).

Outcome of treatment of a feeble breather with Rett syndrome with a Bi-PAP/CPAP.

- Her face does not turn grey or blue.
- Her gross motor ability has improved.
- She is calmer and more attentive.
- She resopnds to people around her with a smile.
- She sleeps better at night.
- Dramatic decrease of seizures.
- Normalisation of colour and temperature of feet (earlier cold and bluish).
- Decrease of cyanosis from several times each day to once in 4 months.
- Normal colour of lips and face.


A
apnoea
Fp1-F7
F7-T3
T3-T5
T5-O1
Fp2-F8
F8-T4
T4-T6
T6-O2
Fp1-F3
F3-C3
C3-P3
P3-O1
Fp2-F4
F4-C4
C4-P4
P4-O2
Program 1
11:21:37 – 70 Hz, 0.50 Hz, 50 Hz
100 µV
1 sec


B
Fp1-F7
F7-T3
T3-T5
T5-O1
Fp2-F8
F8-T4
T4-T6
T6-O2
Fp1-F3
F3-C3
C3-P3
P3-O1
Fp2-F4
F4-C4
C4-P4
P4-O2
Program 1
12:07:52 – 70 Hz, 0.50 Hz, 50 Hz
12:07:52 Program 1, 30 mm/sec, 100 µV/cm, 70.0 Hz, 0.500 Hz, 50 Hz
100 µV
1 sec

References

- Julu, Witt Engerström, Hansen, Apartopoulos, Engerström, ESRRA group: Treating hypoxia in a feeble breather with Rett syndrome. Brain&Development 2012.

- Julu, Witt Engerström, Hansen, Apartopoulos, Engerström, Pini, Delamont, Smeets: Cardiorespiratory challenges in Rett syndrome.

  The Lancet 2008.

- Julu, Witt Engerström: Assessment of the maturity related brainstem functions reveals the heterogenous phenotypes and facilitates clinical management of Rett syndrome.

  Brain Dev 2005 Nov;27 Suppl 1:S43-53.

- Julu: In Kerr & Witt Engerström (eds): Rett Disorder and the developing brain.

  Oxford University Press 2001; 131-181.

Tissue respiration

- Tissue respiration: Transport from blood vessles to tissue needs energy.
- Energy is made by mitichondria in the cells and needs both oxygen and carbon dioxide at right levels.
- Without adequate oxygen or carbon dioxide tissue, respiration becomes anaerobic – produces a slight amount of energy and causes pain. The body gets progressively week, stiff, ”burnt out”.
- May be understood as progression of the disorder.