Neonatal Neuromonitoring and Neuroimaging

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Advances in fetal and neonatal care reduced mortality in:

- Preterm infants (born <37 weeks gestation)
- Term born critically ill infants

Still many long-term effects of neonatal intensive care on brain development

Neurocognitive profile associated with survivors of preterm birth and term critical illness

Epidemiology

Motor deficits

Learning difficulties

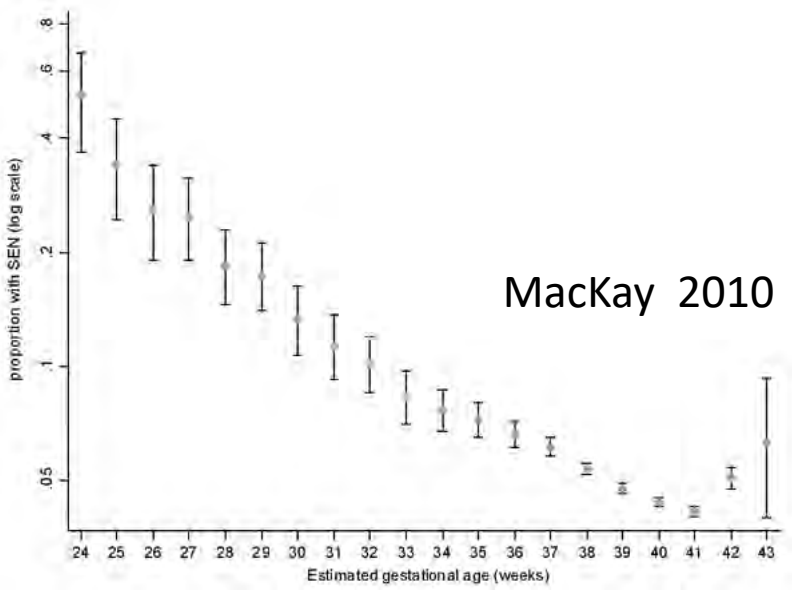
Impairments hearing and vision

Executive function problems

Neuropsychiatric problems

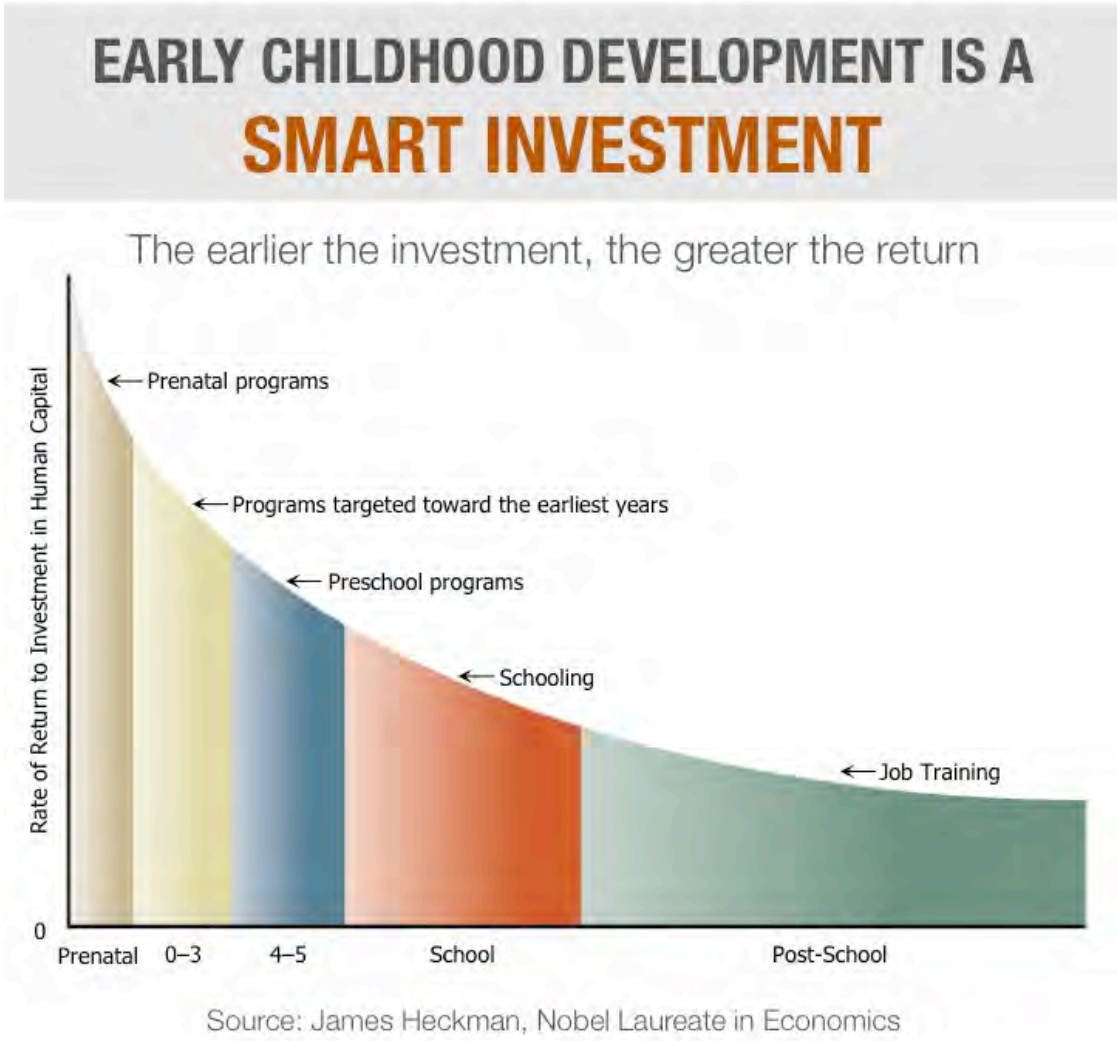
High risk autism spectrum disorder (ASD)

Johnson 2010, Volpe 2009, Guy2015, Gray 2015

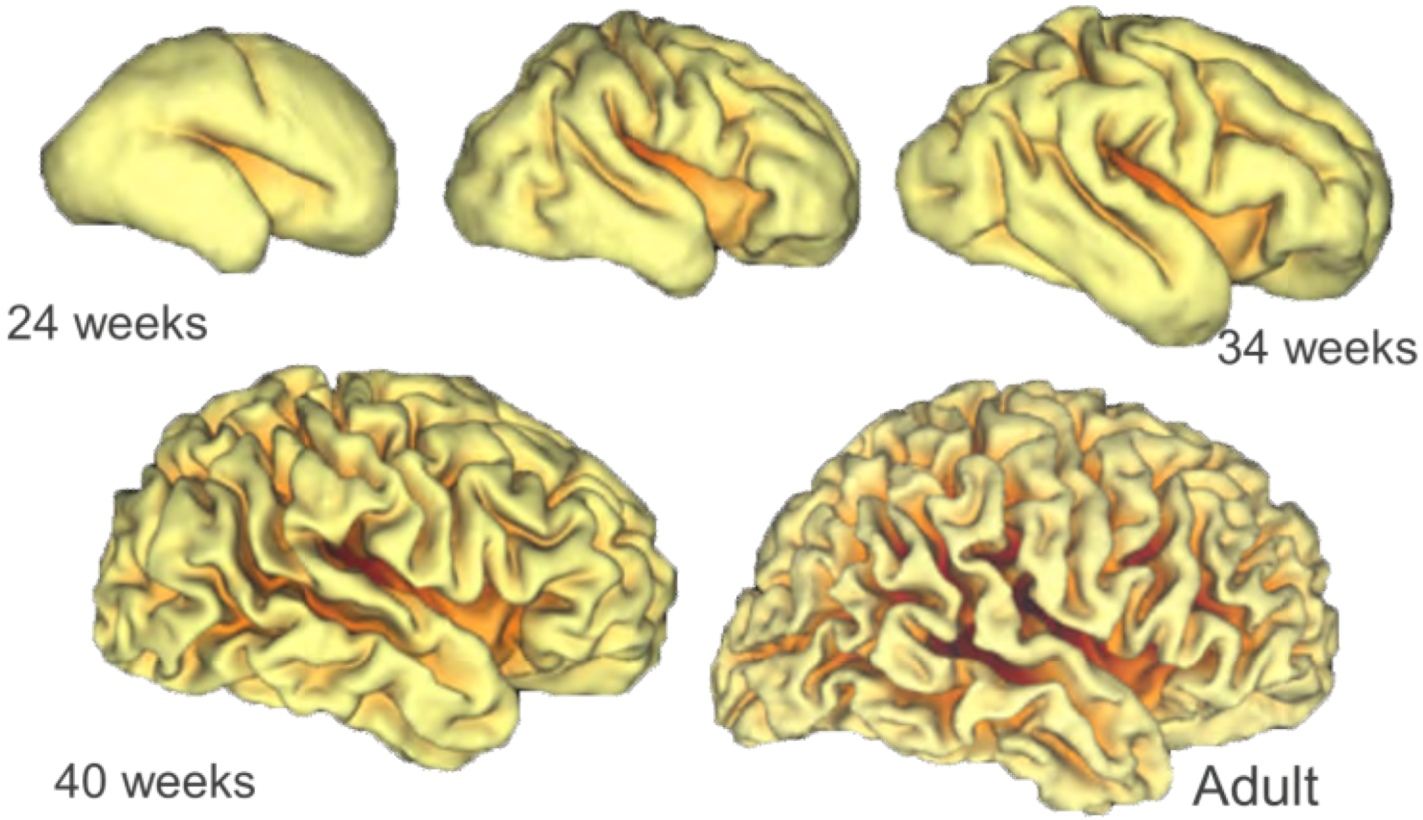


MacKay 2010

Early brain injury has a major socio-economic impact



Preterm birth and brain development



We adjust treatment to our outcome findings

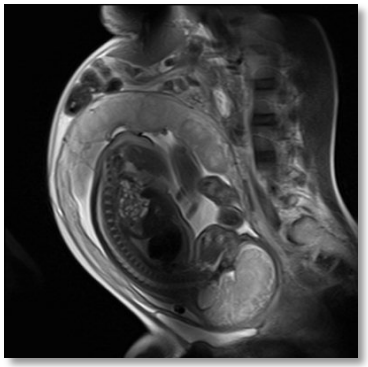
Amiel-Tyson (0-6m)

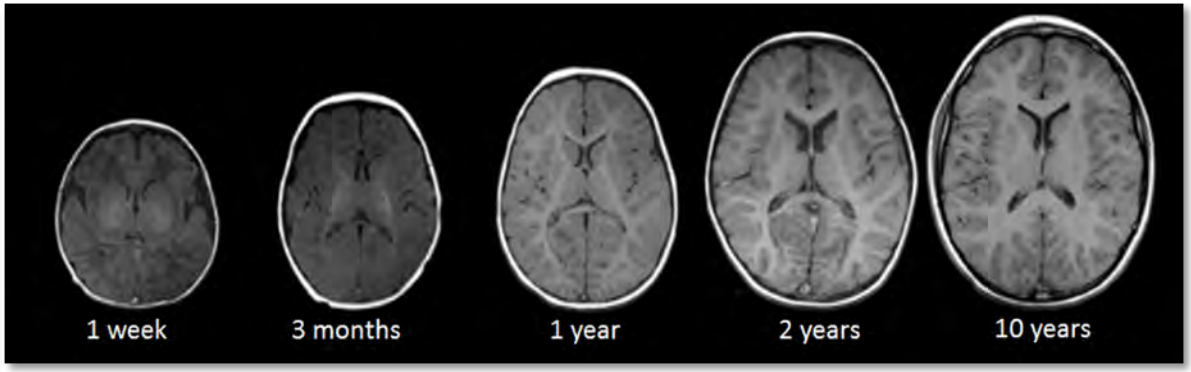
AIMS (0-18m)

GMFCS (0-15y)

Bayley-III-NL (16d-4y)

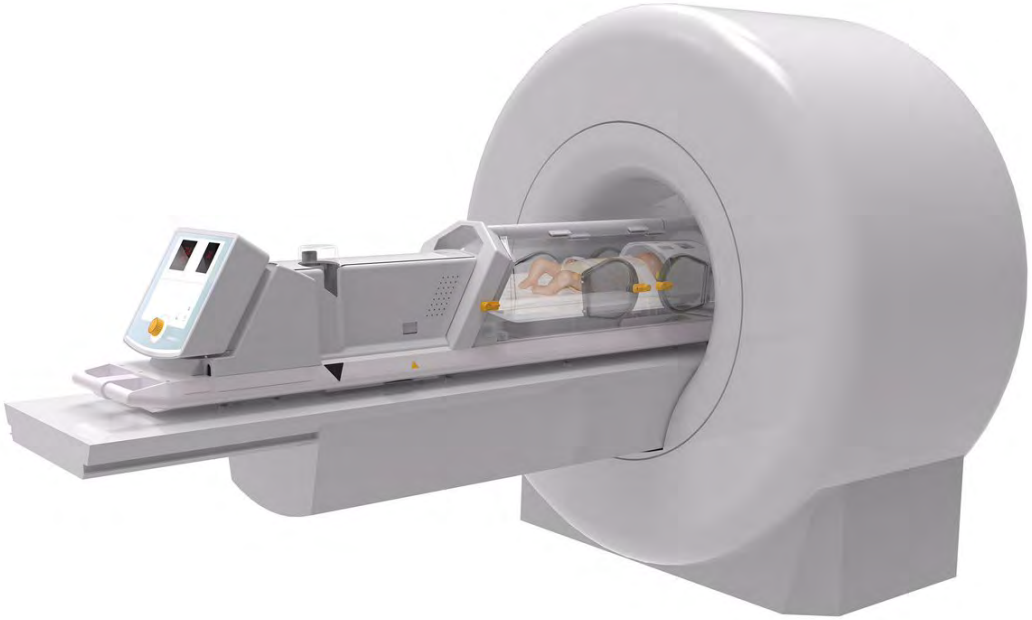
Nepsy-NL (5-12y)





Routine MRI scans

MRI-compatible incubator (LMT)

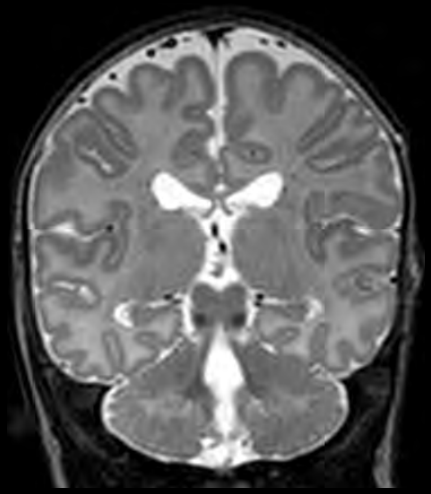


Philips 3Tesla MRI scanner

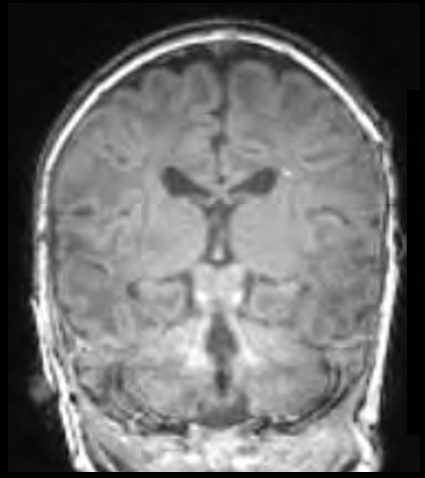
Patient protection and monitoring

50mg/kg chloralhydrate oral

Routine Term MRI duration: 40 min

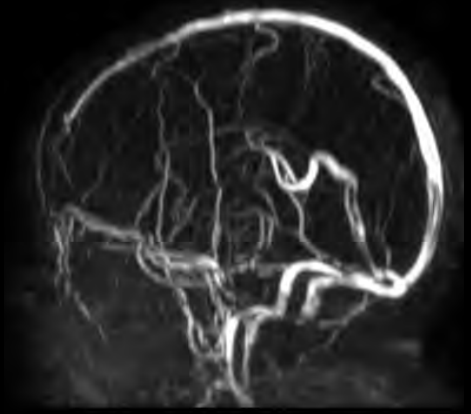


T2-weighted

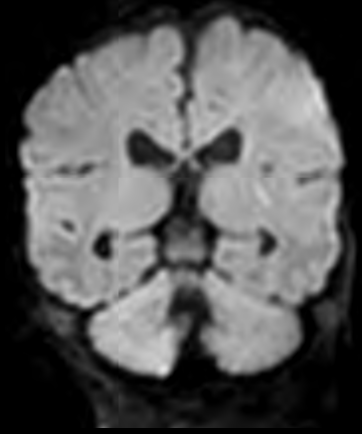


T1-weighted (3D)

MRA



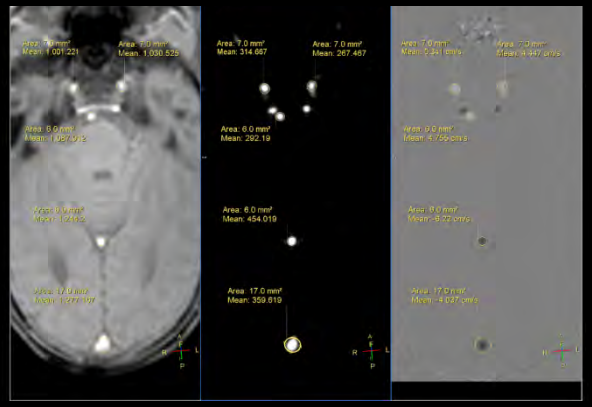
MRV



DWI

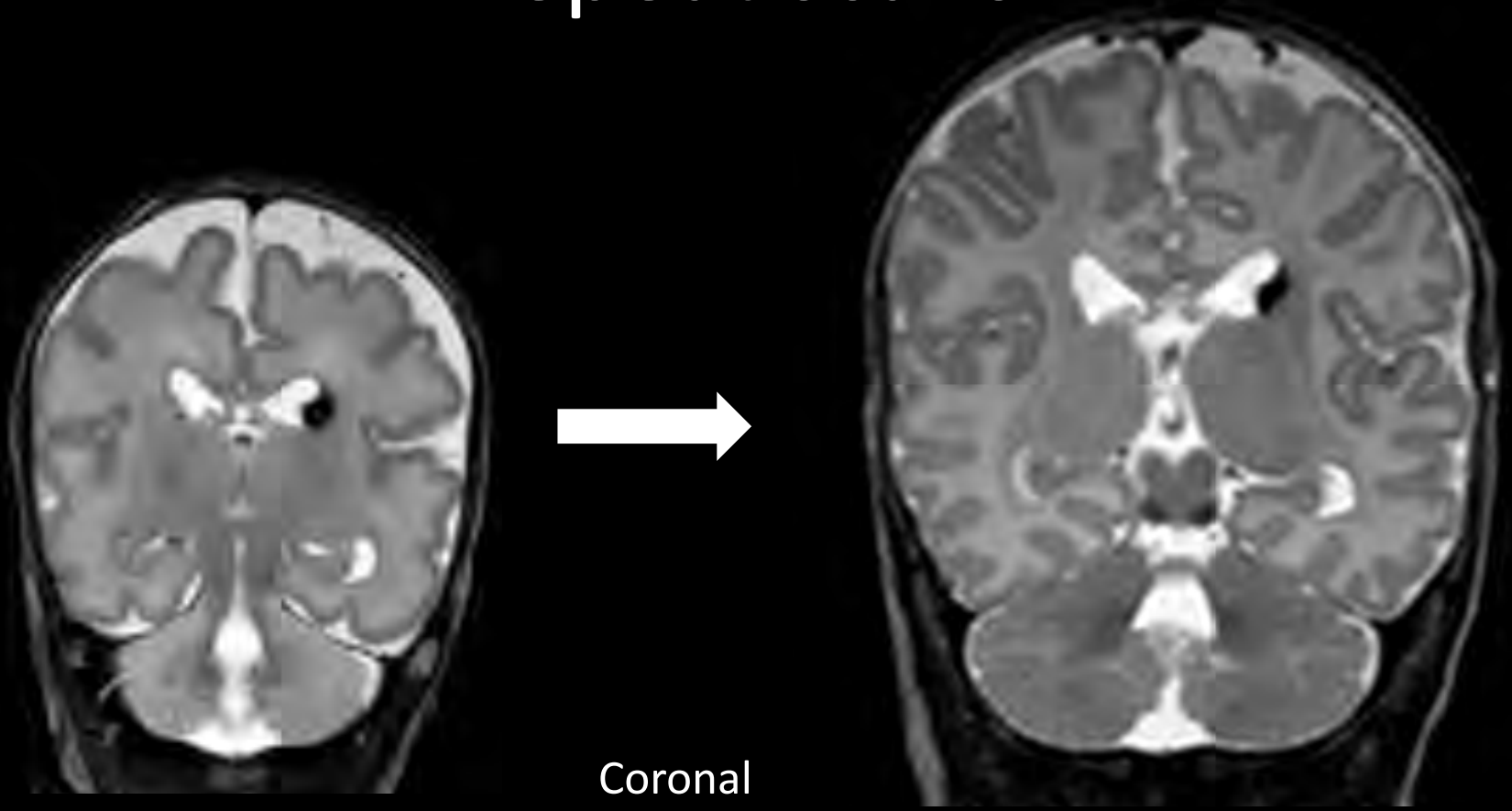
FA-Map (DTI)

SWI



Flow measurements

Repeat scans

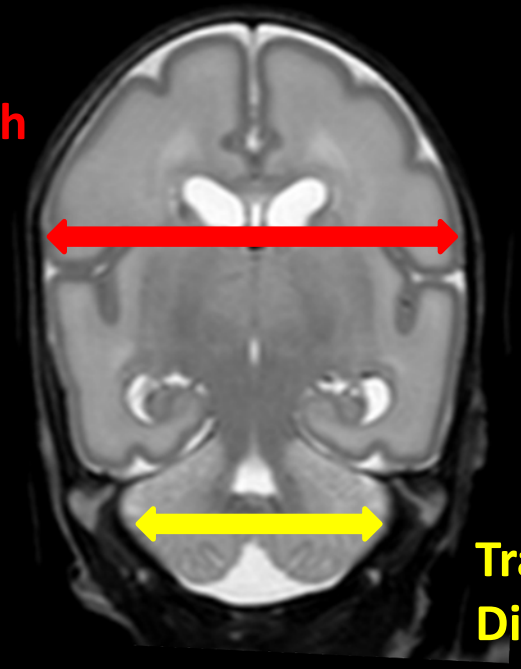


Coronal
T2-w scans

30 weeks

40 weeks

Biparietal width

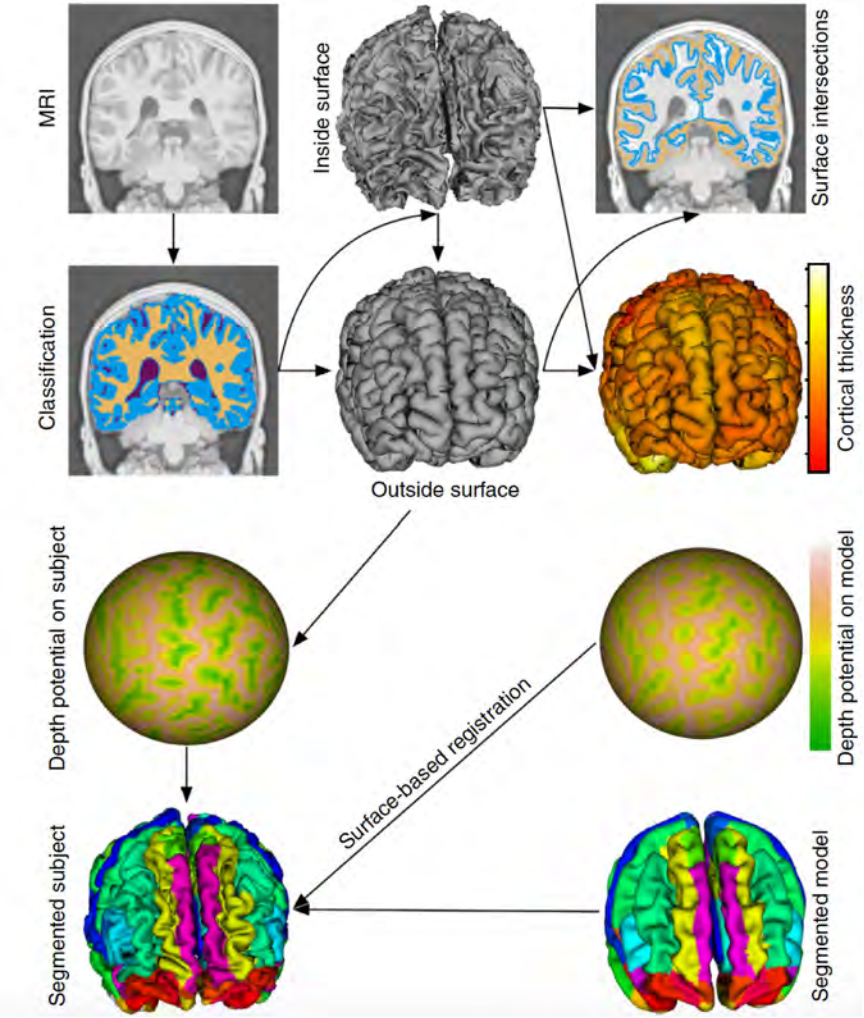


Transcerebellar Diameter

Interhemispheric distance

Deep Gray Matter Area

Postprocessing T1w- and T2w scans



Lerch 2017

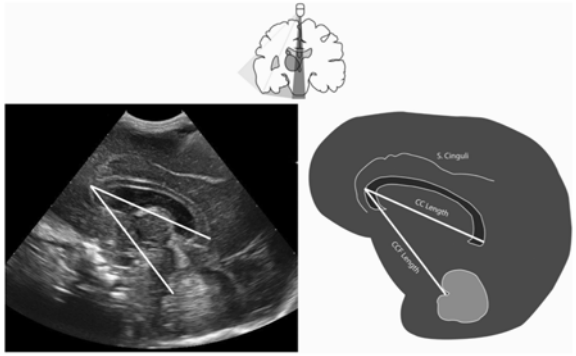
Surface-based analyses.

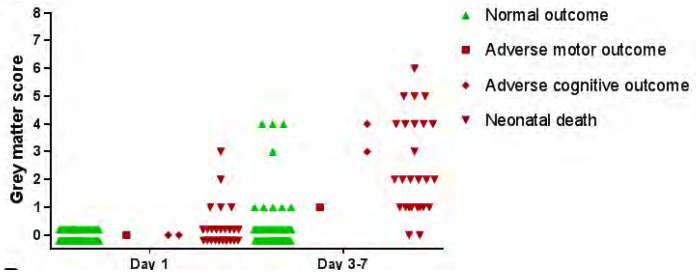
The inside and outside surfaces of the cortex are extracted

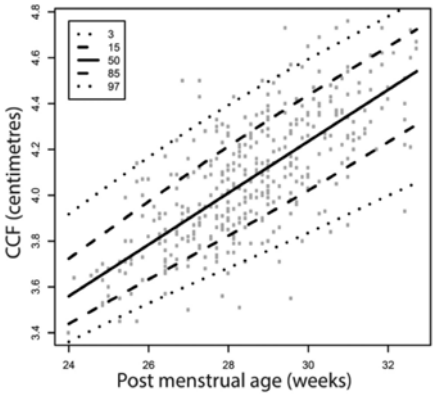
Cortical thickness can be computed based on the distance between the inside surface and outside surface, and surface area computed on either surface

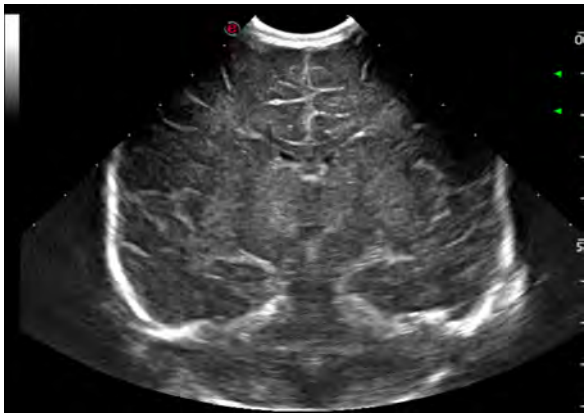
Ultrasound
2D Measurements / Injury scores

Ultrasound





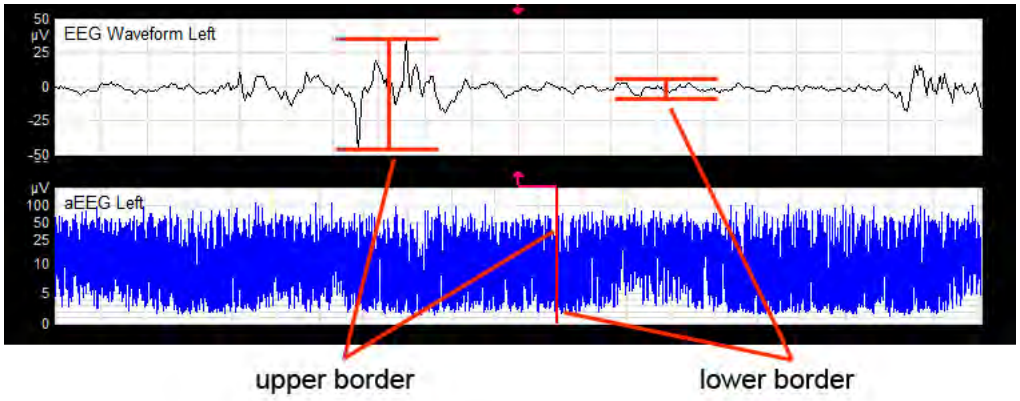


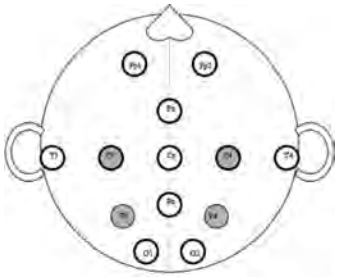


Annink, Ped Research, 2020

Roelants, AJNR, 2016

Amplitude Integrated EEG





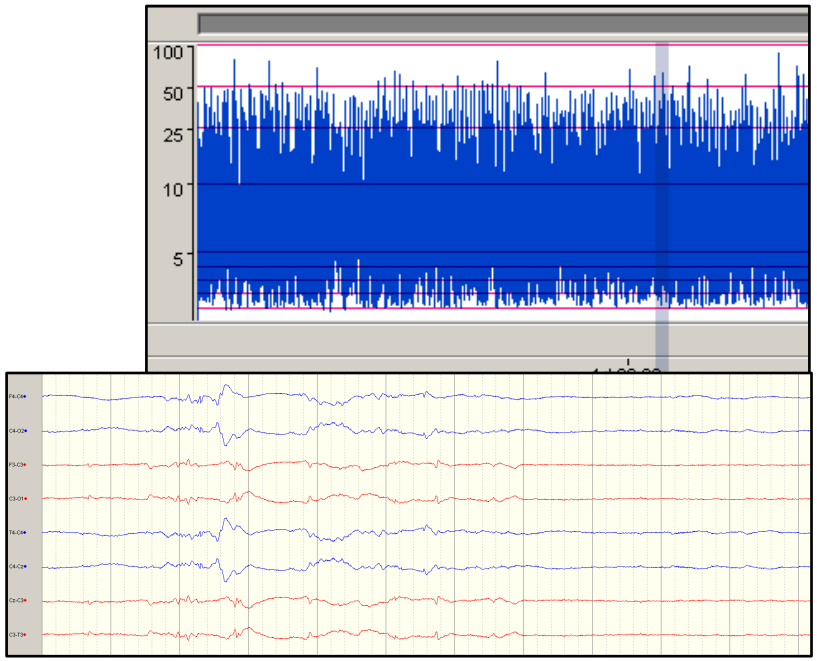
Hellstrom-Westas, Acta Ped, 2014
Burn, Jove, 2017

aEEG/EEG Background Patterns

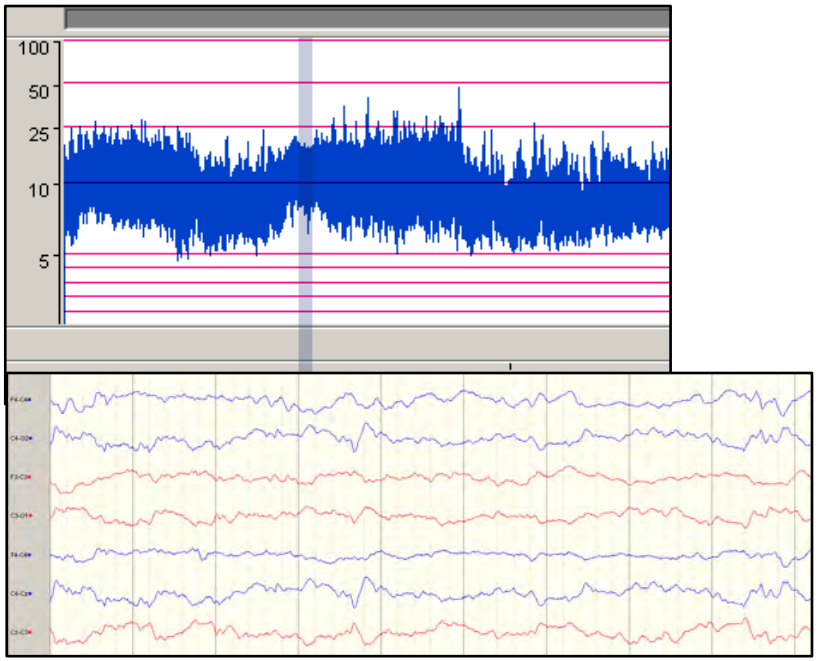
Changes with gestational age

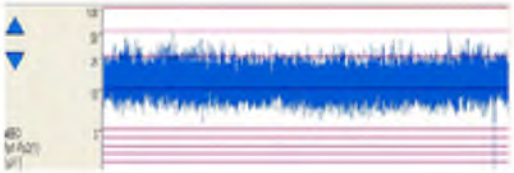
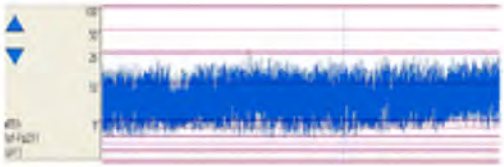
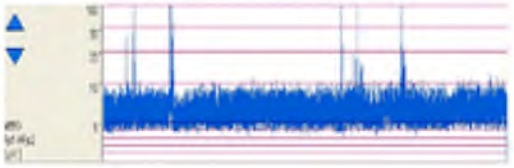
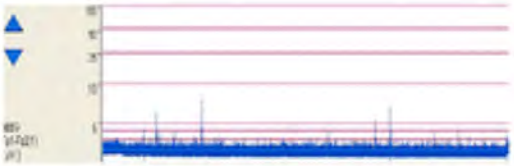
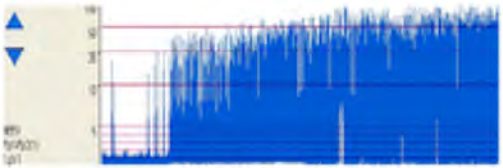
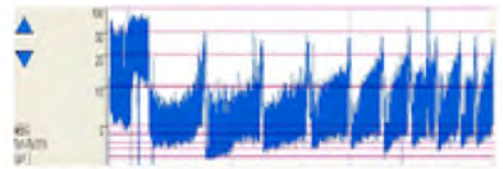
- Increasing continuity
- Decreasing IBI
- Increasing variability (sleep-wake cycling)

Preterm



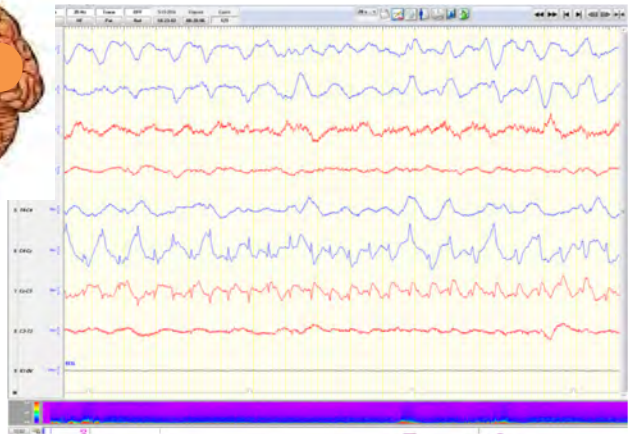
Term



Continuous normal voltage		Maximum >10 µV Minimum >5 µV	Continuous background activity with voltage 10–25 (50) but without sleep stages
Discontinuous normal voltage		Maximum >10 µV Minimum ≤5 µV	
Low voltage		Maximum ≤10 µV	Around 5 µV
Flat		Isoelectric activity	<5 µV
Burst suppression		Bursts of high voltage >25 µV Absent activity <2 µV	High voltage (>30 lV) delta (0.4–4 Hz) and theta (4–8 Hz) lasting 1–10 s with suppressed activity of <5 lasting >2 s
Status epilepticus		Diagnosed together with raw electroencephalography trace	

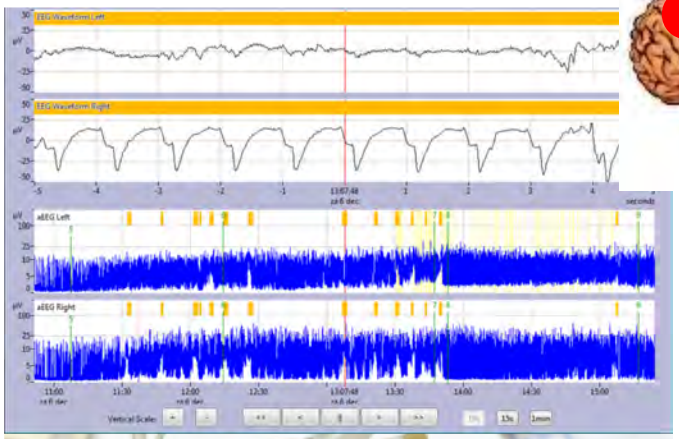
Seizure detection

Standard EEG

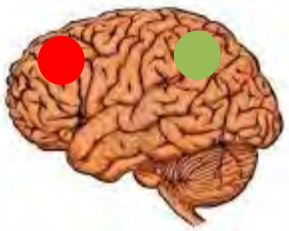


Seizure detection: 100%

aEEG



Seizure detection: 86-94%



Dependent on:

- Experience reviewer
- Number of channels (more=better)
- Use raw EEG

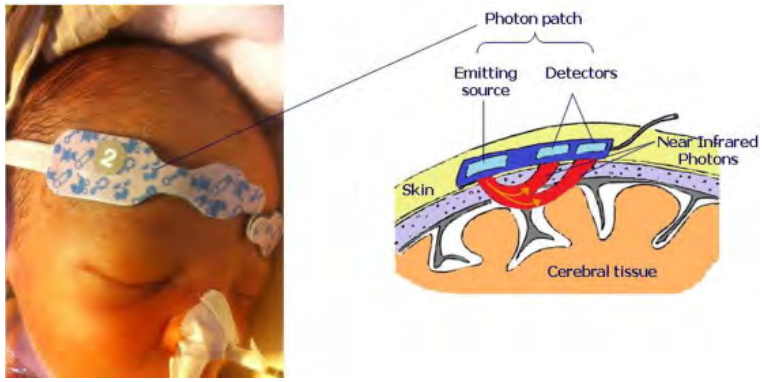
Rakshasbhuvankar et al. Seizure 2015

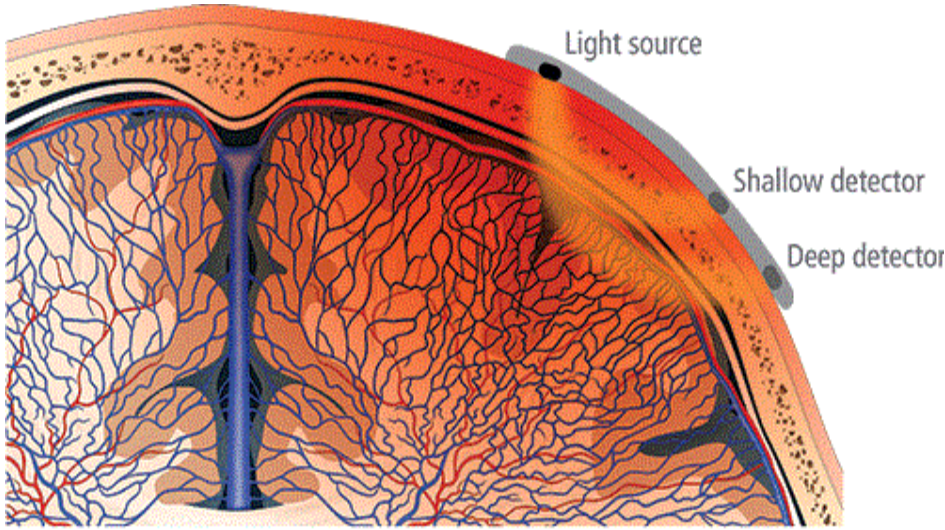
Near Infrared Spectroscopy

Mostly small vasculature[1]
- Arterioles
- Capillaries
- Venules

Cerebral blood volume[2]
- 25% arterial
- **75% venous**
- (5% capillaries)

NIRS takes it all
- SO_2 in combined arterial-capillary-venous compartment





[1] Liu H et al. Phys Med Biol 1995, [2] An H and Lin W Magn Reson Med 2002.

Low NIRS values/decline

Cardiovascular

- Blood pressure
- PDA
- Hemoglobin
- Venous outflow

Respiratory status

- Low CO_2
- Ventilation pressures
- FiO_2 /SaO_2

Brain

- Stroke/HIE early (term)

Other

- Hematoma
- Hydrocefalus

High values/increase

Cardiovascular

- High inotropes?

Respiratory status

- High FiO_2
- High CO_2

Brain

- Low glucose
- Sedatives
- Stroke/HIE late (term babies)

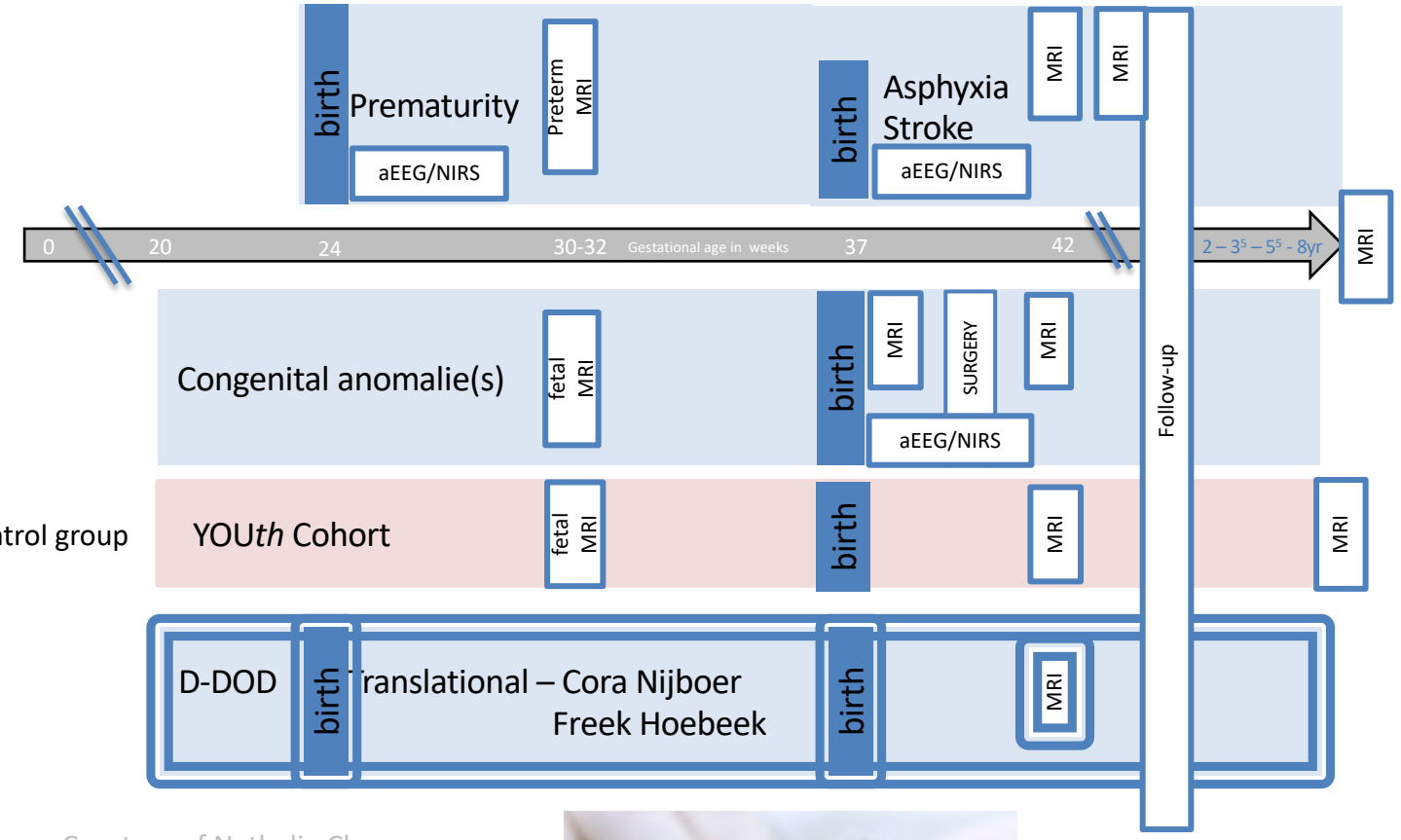
[1] Pellicer et al 2013, [2] Hyttel-Sorensen 2015, [3] Riera et al 2015

Imaging / EEG and follow up showed us what is harmful to the brain

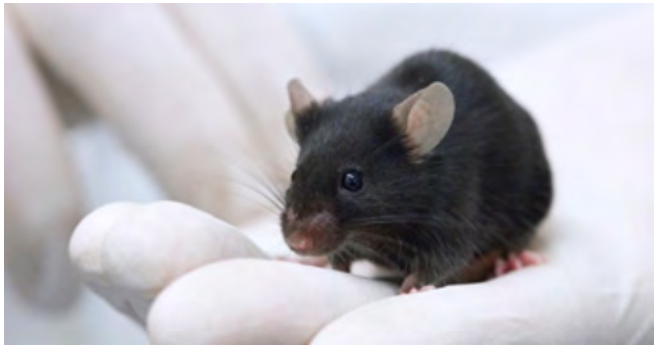
Several risk factors

Hypoxia, Hyperoxia, Inflammation, Hypotension, Steroids…

Department of Developmental Origins Of Disease (DDOD)



Courtesy of Nathalie Claessens



Cerebral blood flow
Energy failure
Hypothermia
Antioxidants
NMDA-2nd messenger modulation
Glutamate release
Calcium dependent excitotoxicity
Apoptotic cell death
Necrotic cell death
Caspase inhibitors
Delayed cell death
Inflammation
Anti-inflammatories
Repair
Growth factors
Restoration
Plasticity and recovery
Stem cells

What we would like to know as clinicians…

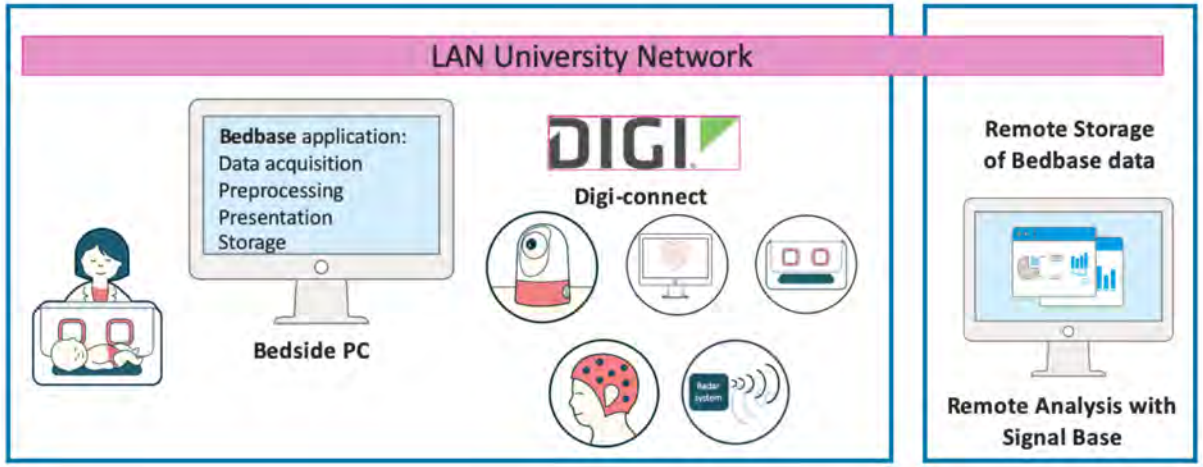
Is the brain maturing appropriately?

We need to steer our treatment: *Is the brain under attack?*
Do I need to increase the inotropes? What is the effect of fluid loading on the brain?

Are we taking the right actions: stress/pain/sleep?

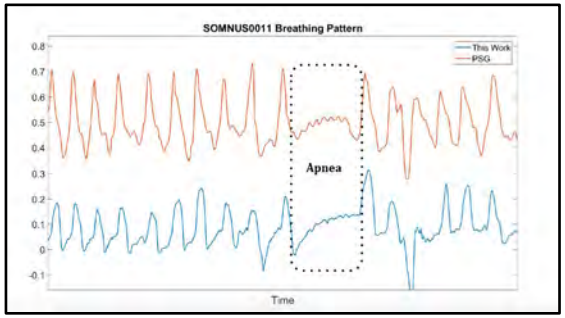
How well does this brain autoregulate?

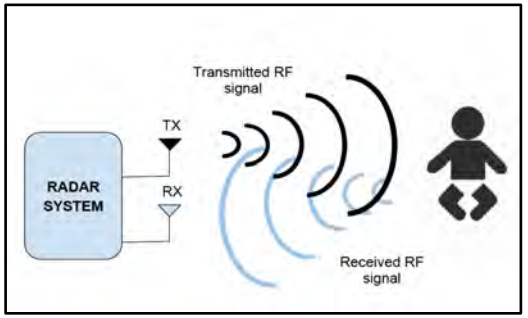
Bedbase

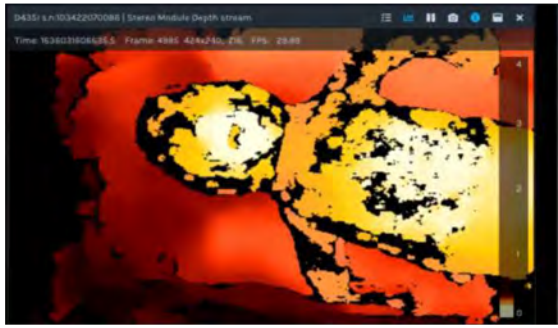

LAN University Network
Bedbase application:
Data acquisition
Preprocessing
Presentation
Storage
Bedside PC
DIGI
Digi-connect
Remote Storage
of Bedbase data
Remote Analysis with
Signal Base

Digital Health Projects

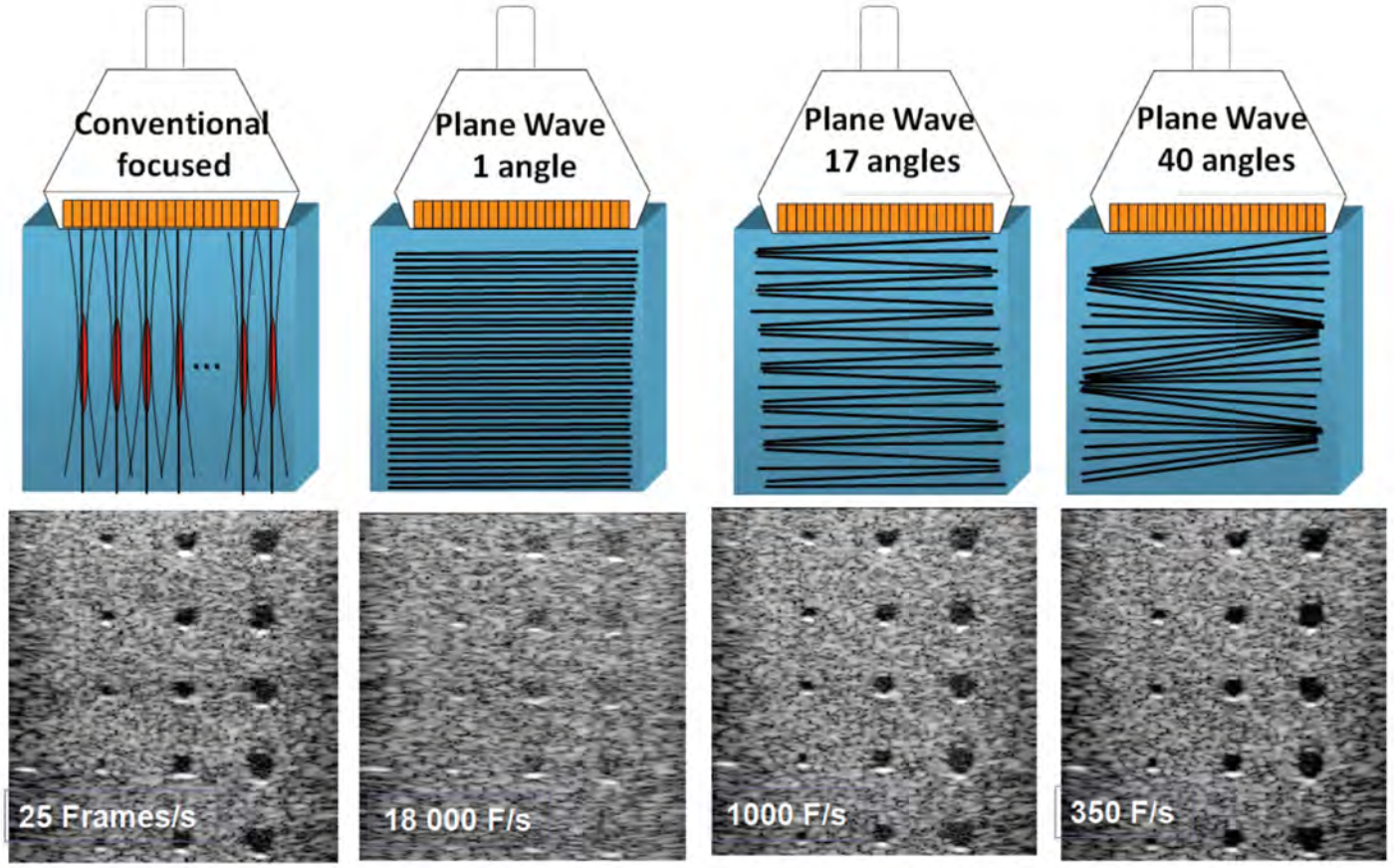
Quantification of behavior





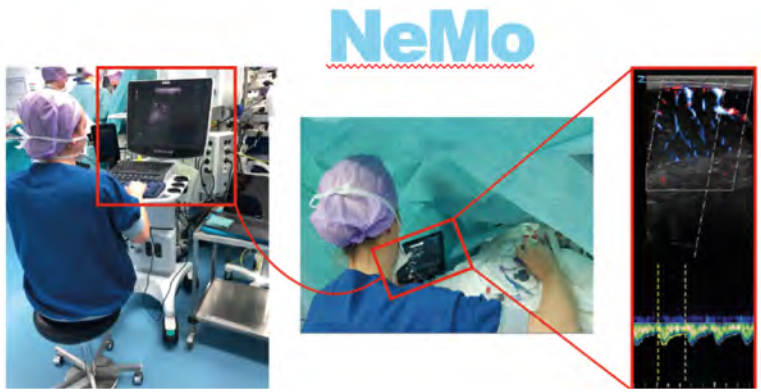


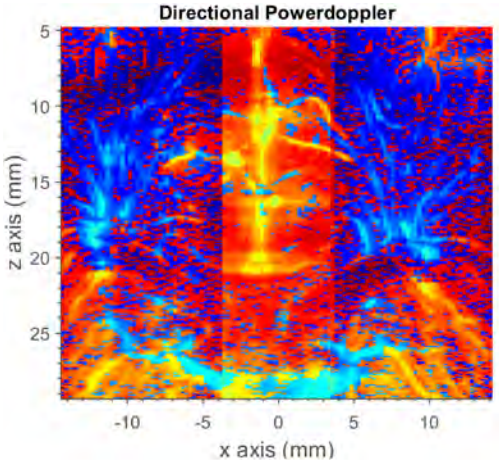
High Frame Rate Ultrasound



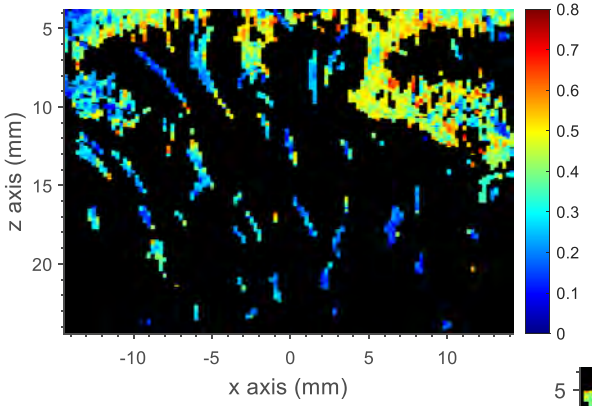
Tanter & Fink 2014

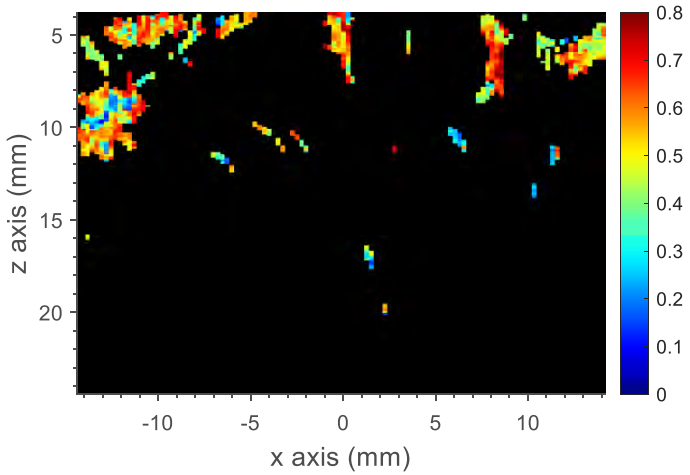
Ultrasound: High Frame Rate Doppler

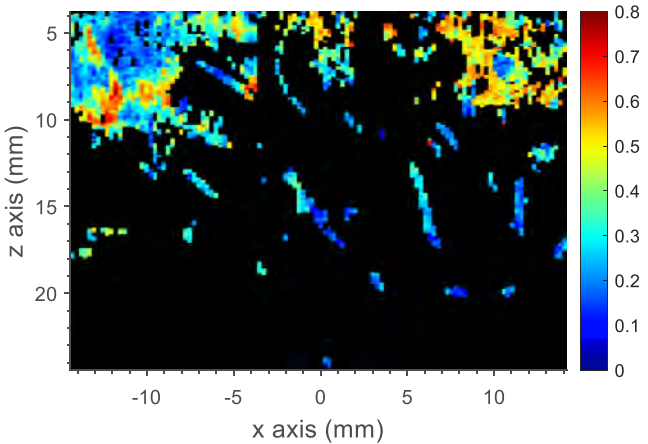




Pre-Peri-Post Noradrenaline





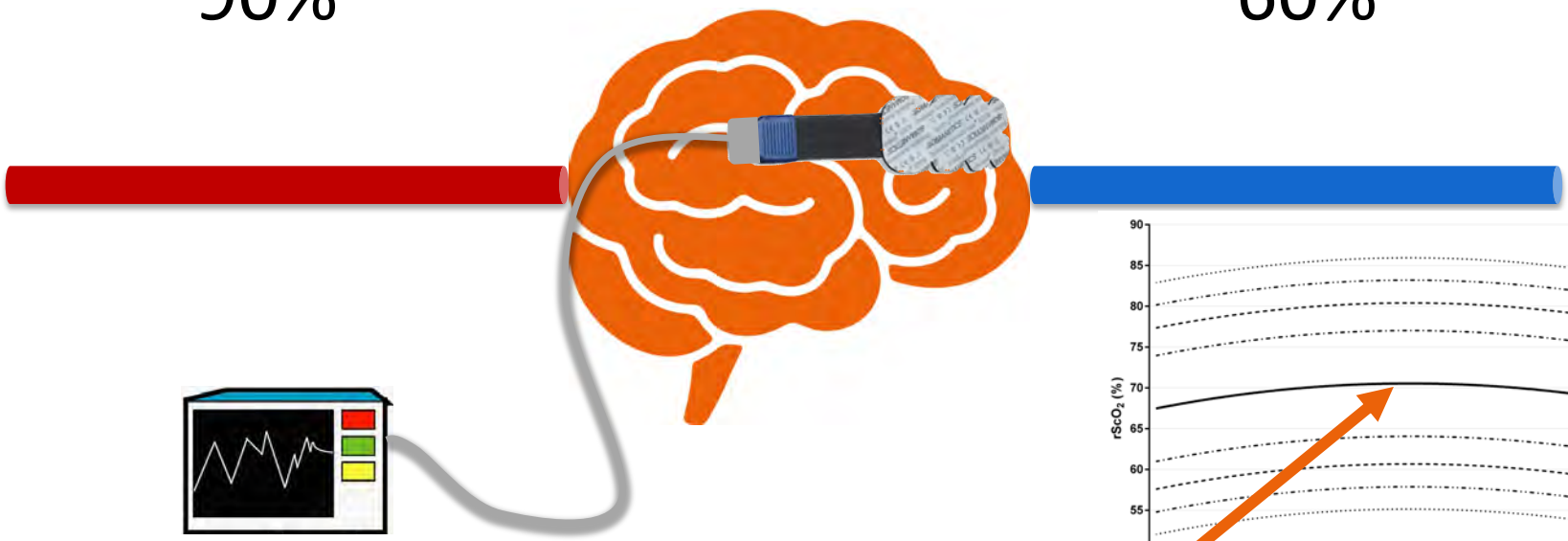


NIRS

¼ Arterial blood
¾ Venous blood

SaO_2
90%

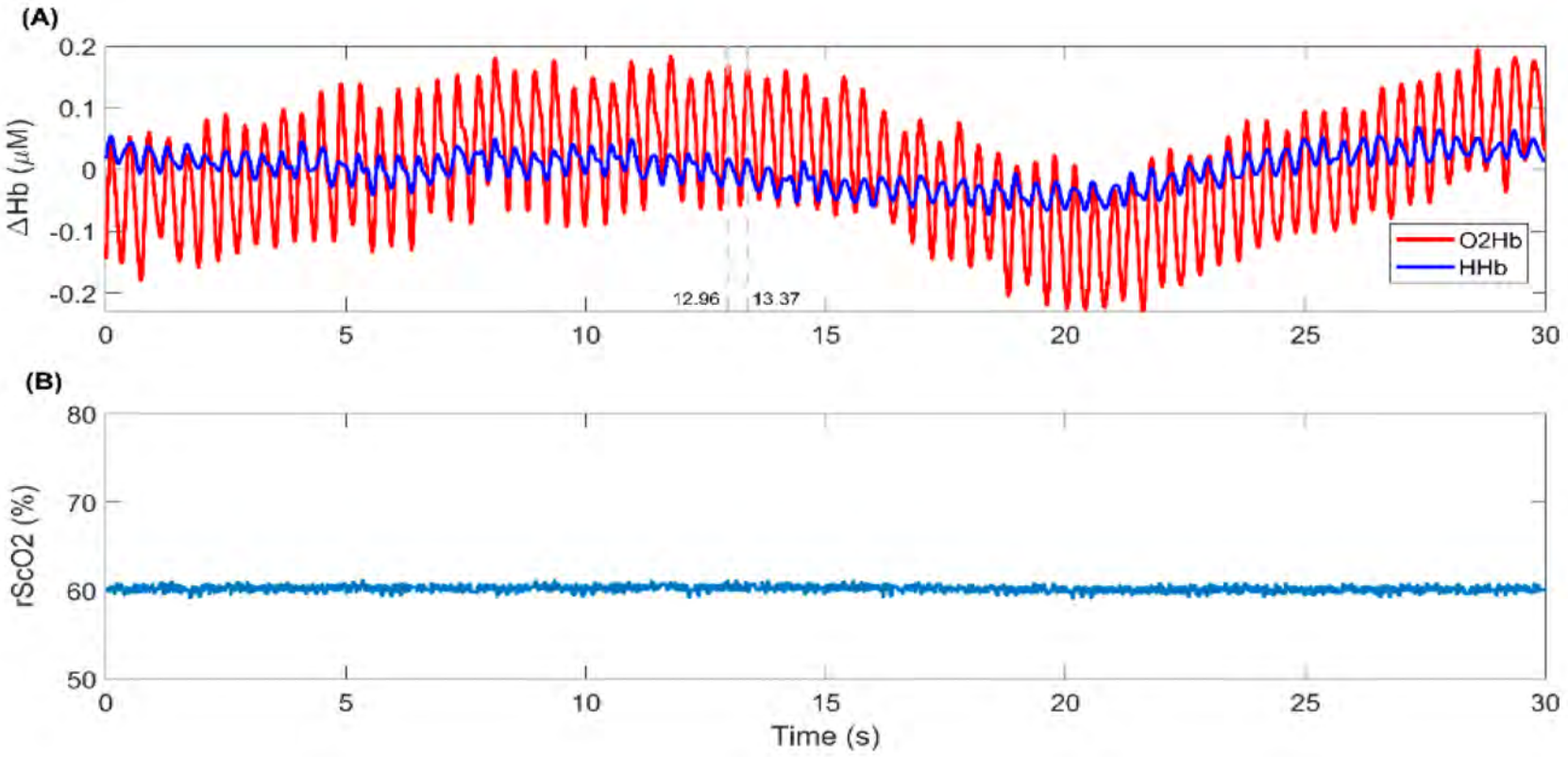
SvO_2
60%



NIRS ($rScO_2$):
¼ x 90%
¾ x 60%

$rScO_2$
67%

High Sampling NIRS



Cerebral vascular autoregulation algorithms
Combination with aEEG
High sampling NIRS -> many possibilities (EEG, beat-to-beat analysis, heart rate estimation, breathing rate estimation, blood pressure analysis)

Infans project

Many thanks for your attention!