

Magnetoencephalography in Infants and young children: Technical and developmental considerations

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- Disclosure: Nothing to disclosure

Why MEG in infants and young children?

- Noninvasive and painless, less anxiety provoking
- Less sensitive to changes in conduction properties during development (skull thickness, sutures) than EEG
- Excellent temporal resolution, reasonable spatial resolution
- Easier to use in group studies to understand developmental/maturational patterns or mechanisms of diseases

➤ Clinical indications

- Epilepsy localization: localization of interictal spikes
- Functional mapping

➤ Research Utility

- Study of normal development
- Plasticity after early brain injury
- Understanding disease mechanisms, predictors of outcome

MEG in Infants and young children

➤ Technical Challenges

- Head movement
- Head size: Distance to sensors
- Recording considerations

➤ Developmental Challenges

- Maturational patterns- Incomplete myelination



- Recording spontaneous MEG–EEG during natural sleep is the preferred option, if attainable, because epileptiform activity is enhanced and untoward drug effects are avoided
- Utilization of hypnotics is not universally accepted as a means of sleep induction. If used, specific annotation of such should be made in the report. The presence of a parent or a staff member within shielded room may be necessary in this situation

American Clinical Magnetoencephalography Society
Clinical Practice Guideline 1: Recording and
Analysis of Spontaneous Cerebral Activity*

*Anto I. Bagić,† Robert C. Knowlton,‡ Douglas F. Rose,§ and John S. Ebersole,||;
for the ACMEGS Clinical Practice Guideline (CPG) Committee***



- Sedation, including general anesthesia, may be necessary to obtain an adequate clinical MEG–EEG recording. These procedures are always performed by an onsite specialized medical team that includes an anesthesiologist physician and/or other licensed provider qualified in anesthesia/sedation, and MEG–EEG personnel should not be a part of this team

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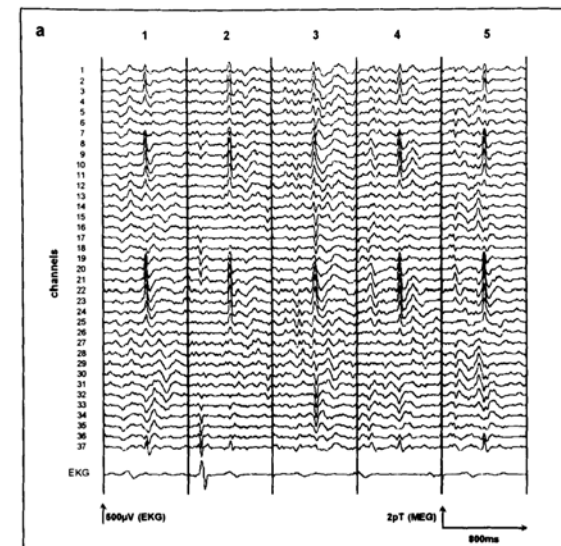


➤ Head movement:

- Young infants- Sleep deprivation, feeding, soothing
- Sedation: Clonidine
- Anesthesia: Dexmedetomidine, Fentanyl, Propofol

- Best approach:
 - Mild sleep deprivation
 - Prepare for the experiment then ask the parents to feed the infant
 - A tight blanket
 - Dim the lights in the recording room
 - Continuous head position monitoring, head movement compensation
 - Or use short blocks (two minutes) and measure the head position before each block

- Oral Clonidine:
- Used frequently for sedation of infants and critically ill children
- Onset around 1 hour, peak in 2-4 hours
- Some data suggest that it enhances detection of focal epileptiform discharges



Intravenous Anesthesia

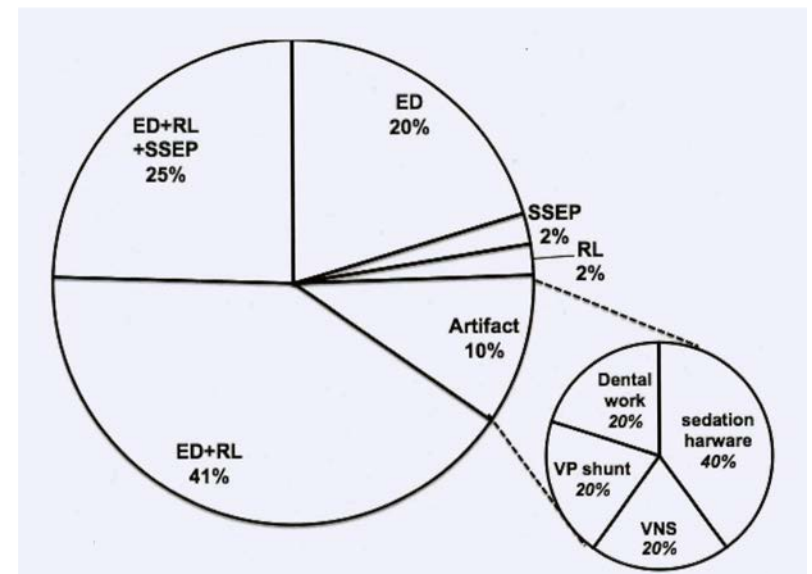
- No established protocol
- Does anesthesia change the proportion of MEG studies with successful detection of interictal epileptiform discharges?
- Does anesthesia affect MEG localization?
- Premedication → Induction → Maintenance
- Most commonly used agent in general is Propofol, GABA agonist
- Propofol increases the inhibition of GABAergic inputs to the thalamus and promotes high-voltage spike and wave spindles and clinical seizures in animal models
- Short duration of action

- Fujimoto et al., 2009
 - Intravenous Anesthesia: Induction with Nitrous oxide, then IV Propofol and remifentanyl
 - Spikes present in 21/28, Clusters in 18 (68%)
 - Seven patients had no spikes, including 60% of non-lesional cases



- Hanaya et al., 2013
 - Repeat MEG studies in the same patients with and without intravenous anesthesia
 - 78% (14/18) had reduction in interictal spikes
 - Patients with clustered MEGSS: same in two (13%), smaller in 8 (53%) and disappeared in four (27%)
 - Propofol significantly reduced the frequency of spikes, more in the irritative than epileptogenic zone

- Birg et al., 2013
 - 49 patients
 - No premedication, Propofol for anesthesia
 - Epileptiform discharges detected in 86%



- Balakrishnan et al., 2007
 - mixed adult and pediatrics
 - Majority induced with Ketamine, maintained with Propofol
 - 74% had interictal discharges , compared to 80% of other children without anesthesia

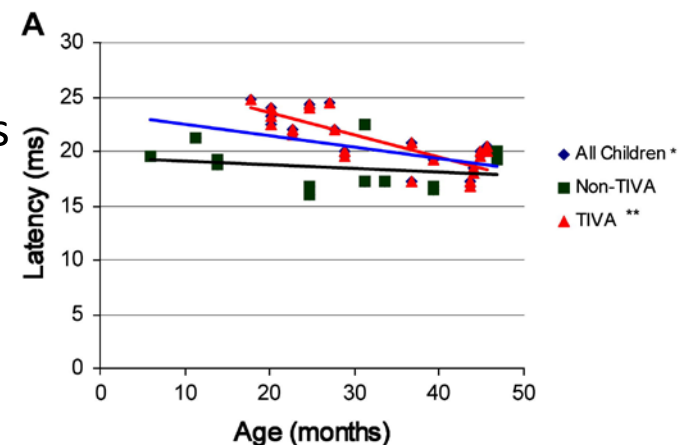


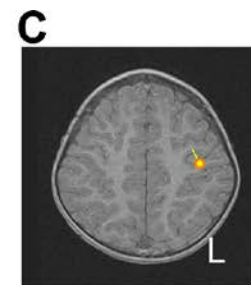
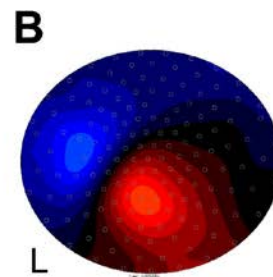
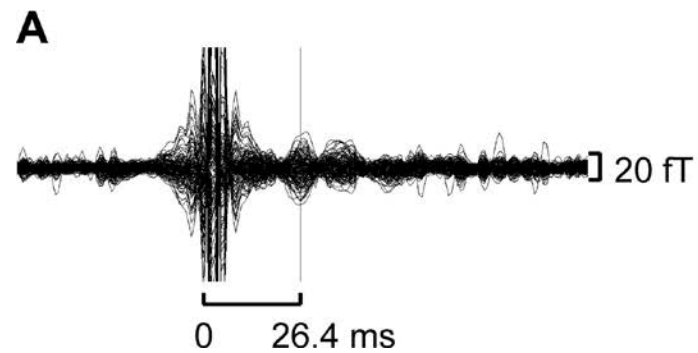
- König et al., 2009,
 - 19 patients: 7 with Propofol, 12 with Dexmedetomidine (an alpha-2 adrenergic agonist) or sevoflurane. Some requiring additional boluses of Propofol
 - dexmedetomidine infusions are preferable to Propofol-based techniques for pediatric MEG scans due to the absence of adverse effect on interictal activity



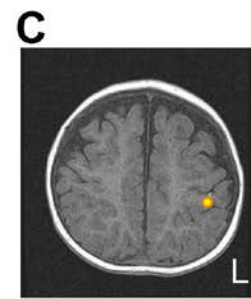
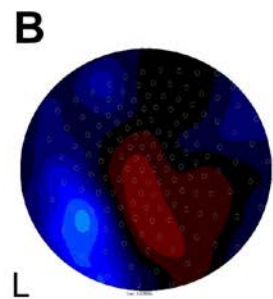
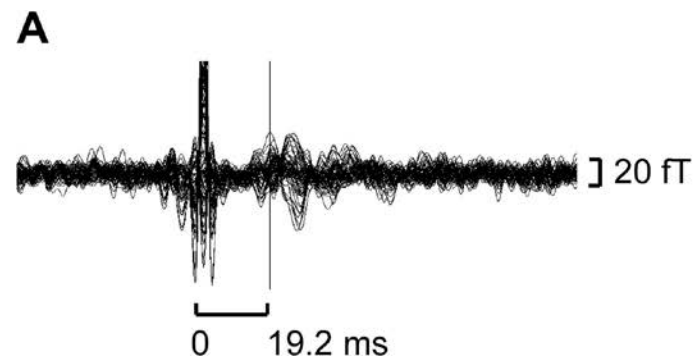
Functional Mapping under Intravenous anesthesia

- Bercovici et al., 2008
- Sensory evoked fields to Median Nerve Stimulation
 - Nitrous oxide for comfort and ease
 - IV Propofol and Remifentanyl for induction. Propofol as maintenance. Remifentanyl reduced to lowest doses
 - Reliable SEF was detected in 77% of a total of 26 patients younger than 4 years old



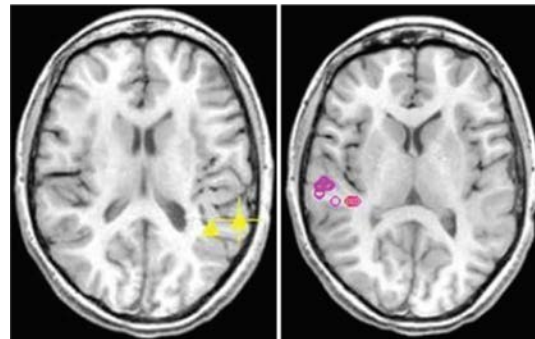


With Anesthesia



Without Anesthesia

- Rezaie et al., 2014, Van Poppel et al., 2012
- 49 sedated patients, 18 months–15 years of age. Passive language mapping
- Localization of receptive language cortex and determination of laterality in 78% of patients
- Proportion of patients deemed left hemisphere dominant for receptive language did not differ between non-sedated and sedated patients, exceeding 90%



FDA Drug Safety Podcast: FDA approves label changes for use of general anesthetic and sedation drugs in young children



Welcome to the FDA Drug Safety Podcast for health care professionals from the Division of Drug Information. This is Lesley Navin, Advanced Practice Nurse.

On April 27, 2017 FDA notified the public that we have approved previously announced label changes regarding the use of general anesthetic and sedation medicines in children younger than 3 years. These changes include:

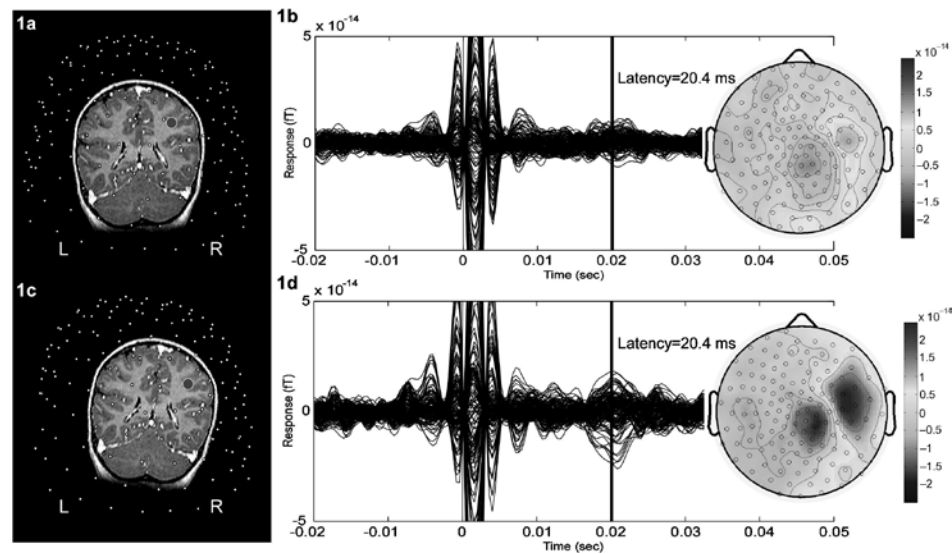
- A new Warning stating that exposure to these medicines for lengthy periods of time or over multiple surgeries or procedures may negatively affect brain development in children younger than 3 years.
- And, additional information to the sections of the labels about pregnancy and pediatric use to describe studies in young animals and pregnant animals that showed exposure to general anesthetic and sedation drugs for more than 3 hours can cause widespread loss of nerve cells in the developing brain; and studies in young animals suggested these changes resulted in long-term negative effects on the animals' behavior or learning.

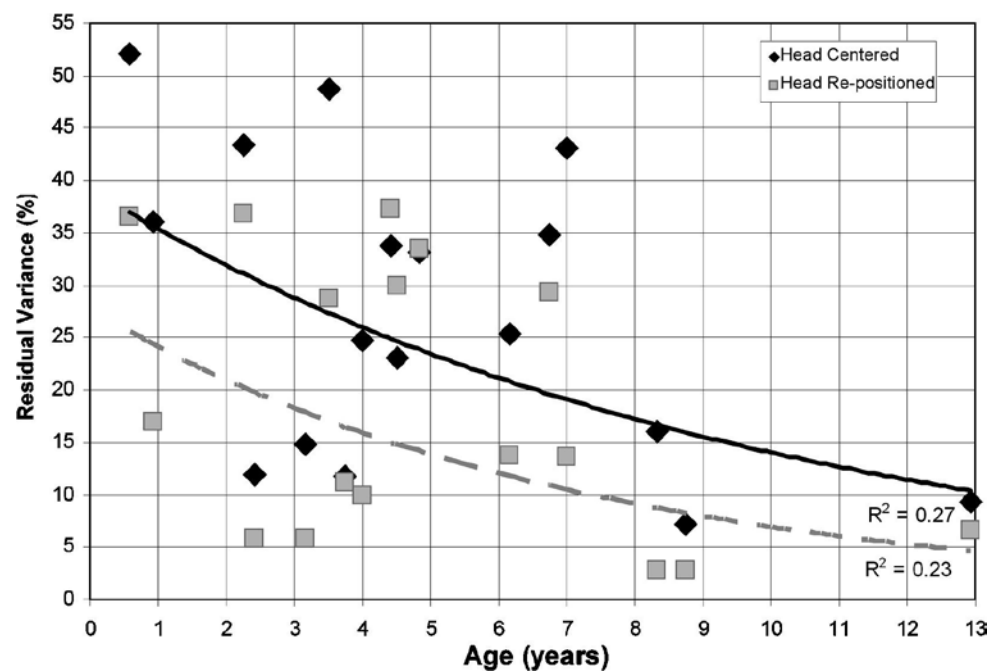
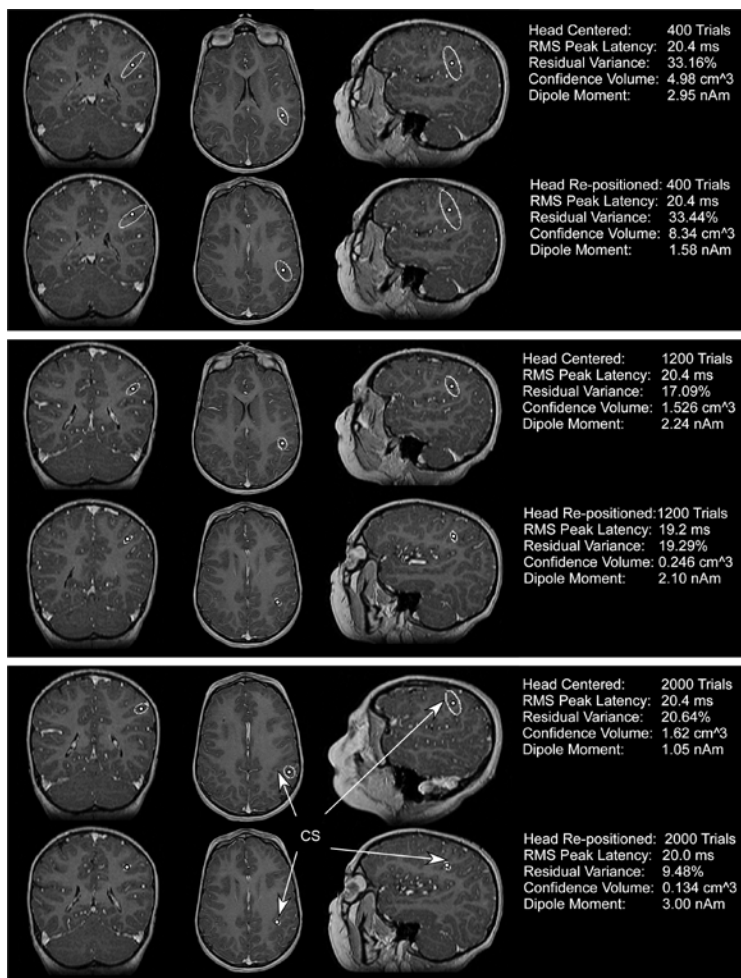


Distance to MEG sensors

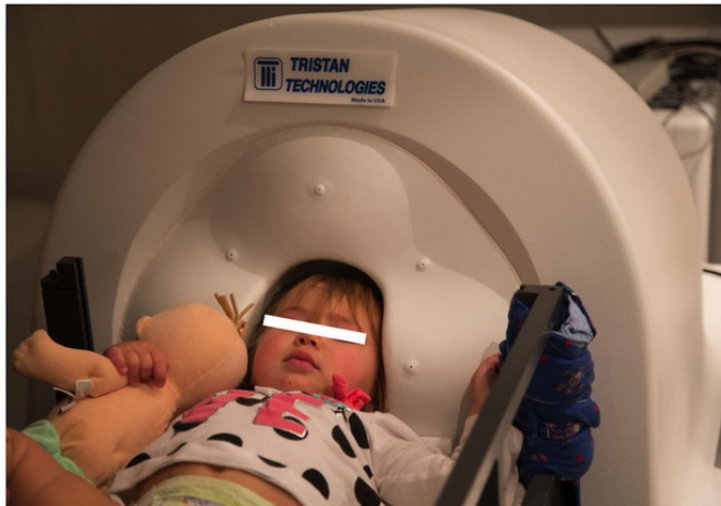
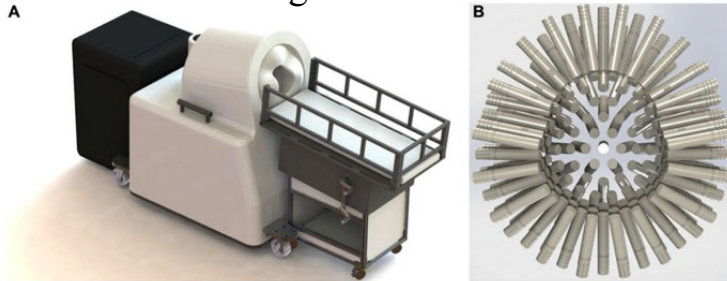
- Current helmet-shaped MEG instruments with 122 to more than 300 channels are optimized for adult head sizes
- The distance between the MEG sensors and the brain is larger in helmet-MEG studies than in adults
- Smaller heads allow for unavoidable larger head movements in children and infants
- Possible solutions:
 - Head positioning in scanner- pads
 - Larger number of trials for evoked responses
 - Smaller helmets
 - OPMs

- 17 infants and children under intravenous anesthesia
- Head circumference ranged from 46 to 53 cm





Artemis 123 biomagnetometer



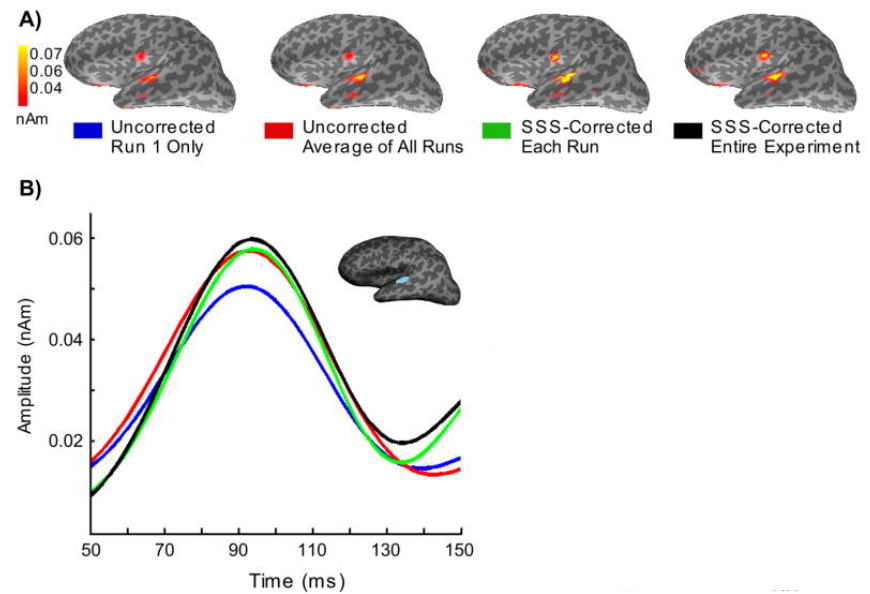
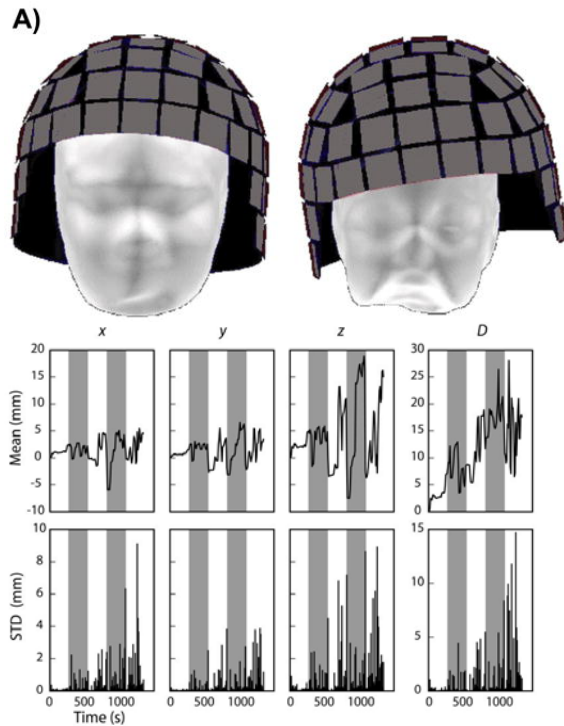
Roberts TP et al., Front Hum Neuroscience 2014



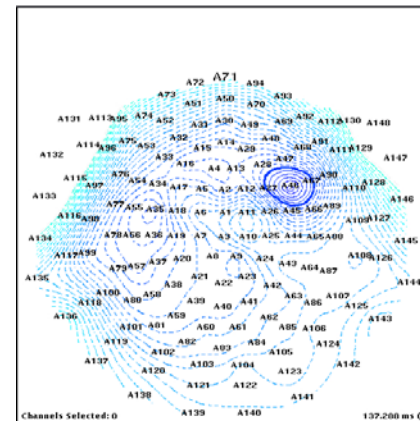
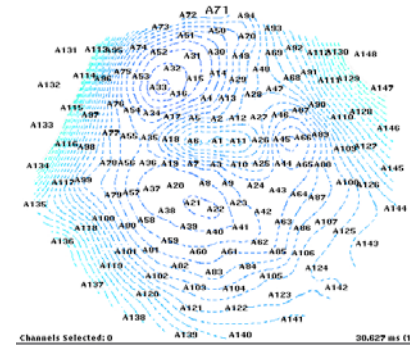
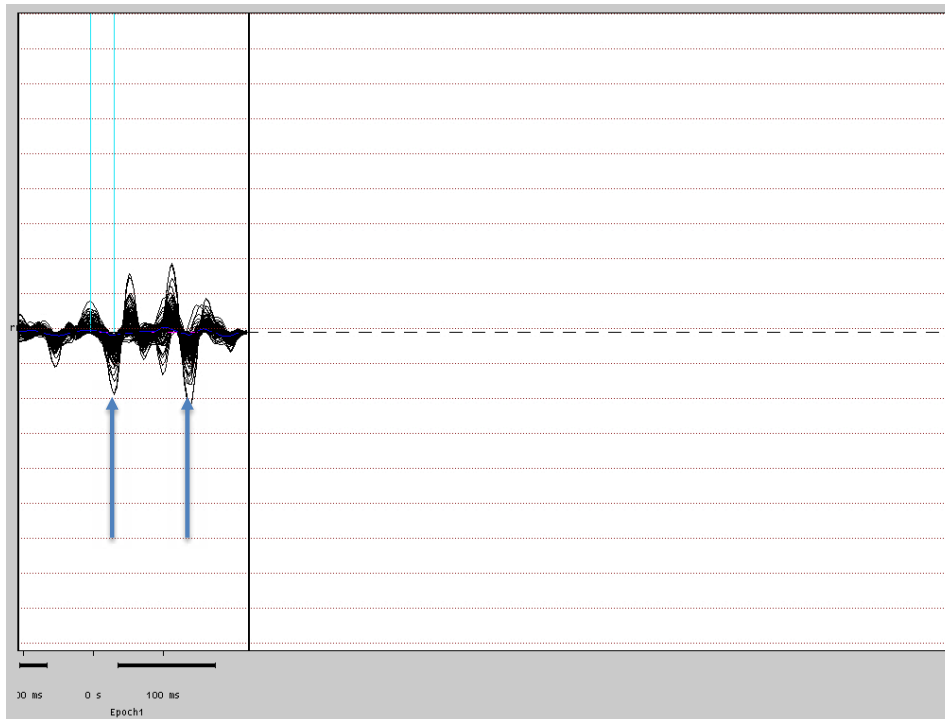
375-channel, whole-head pediatric MEG system ("BabyMEG")

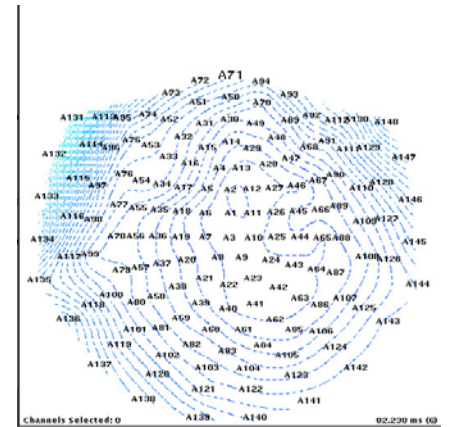
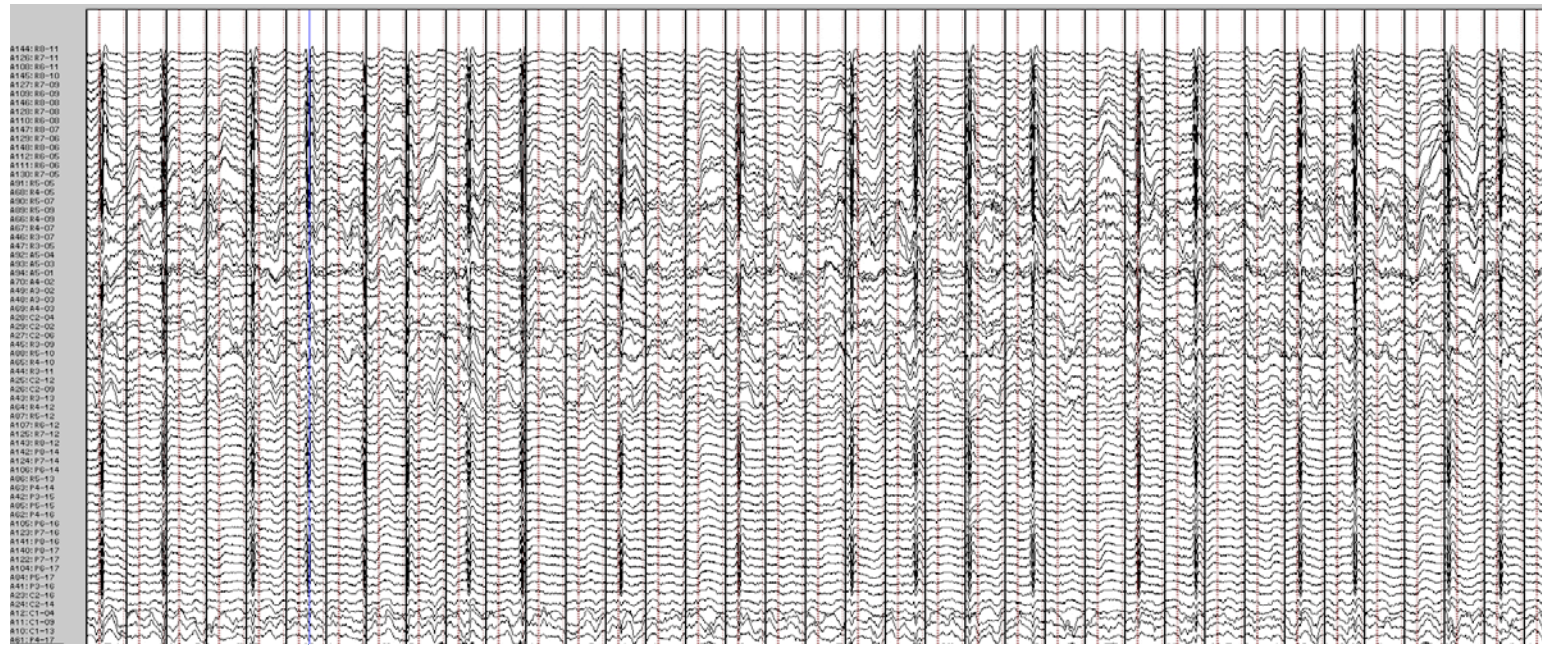
Yoshio Okada; et al., Review of Scientific Instruments 2016

Head Movement

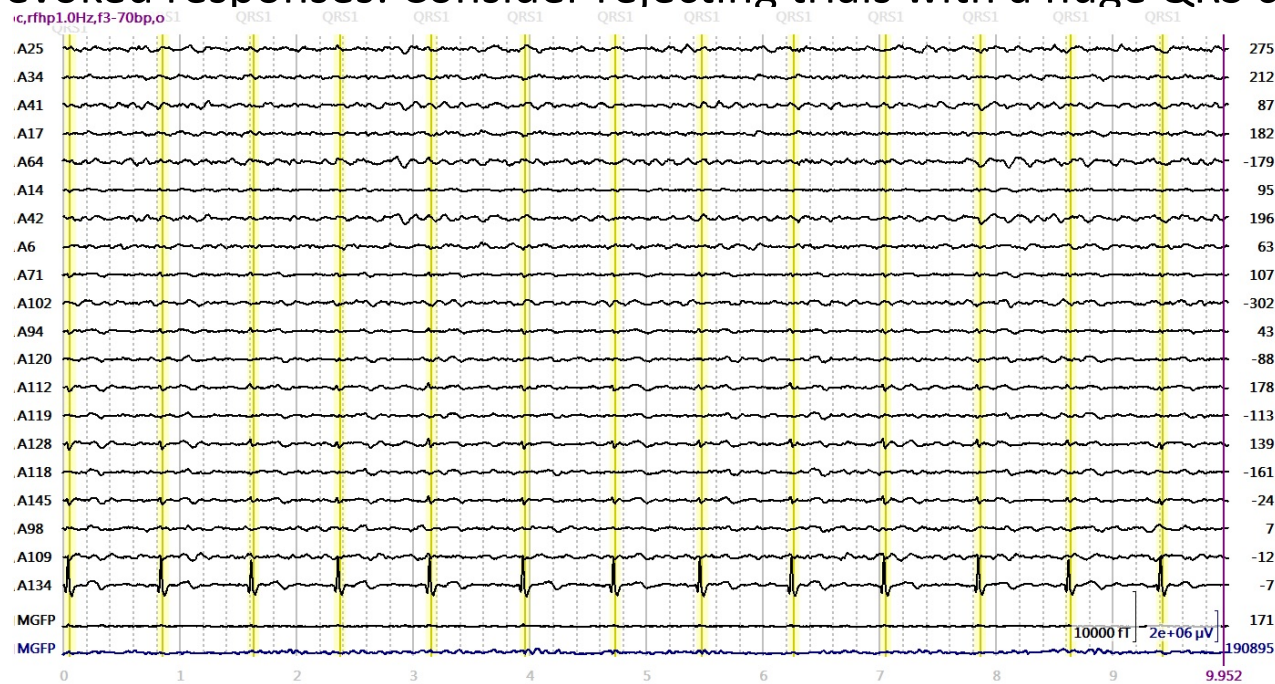


Artifacts

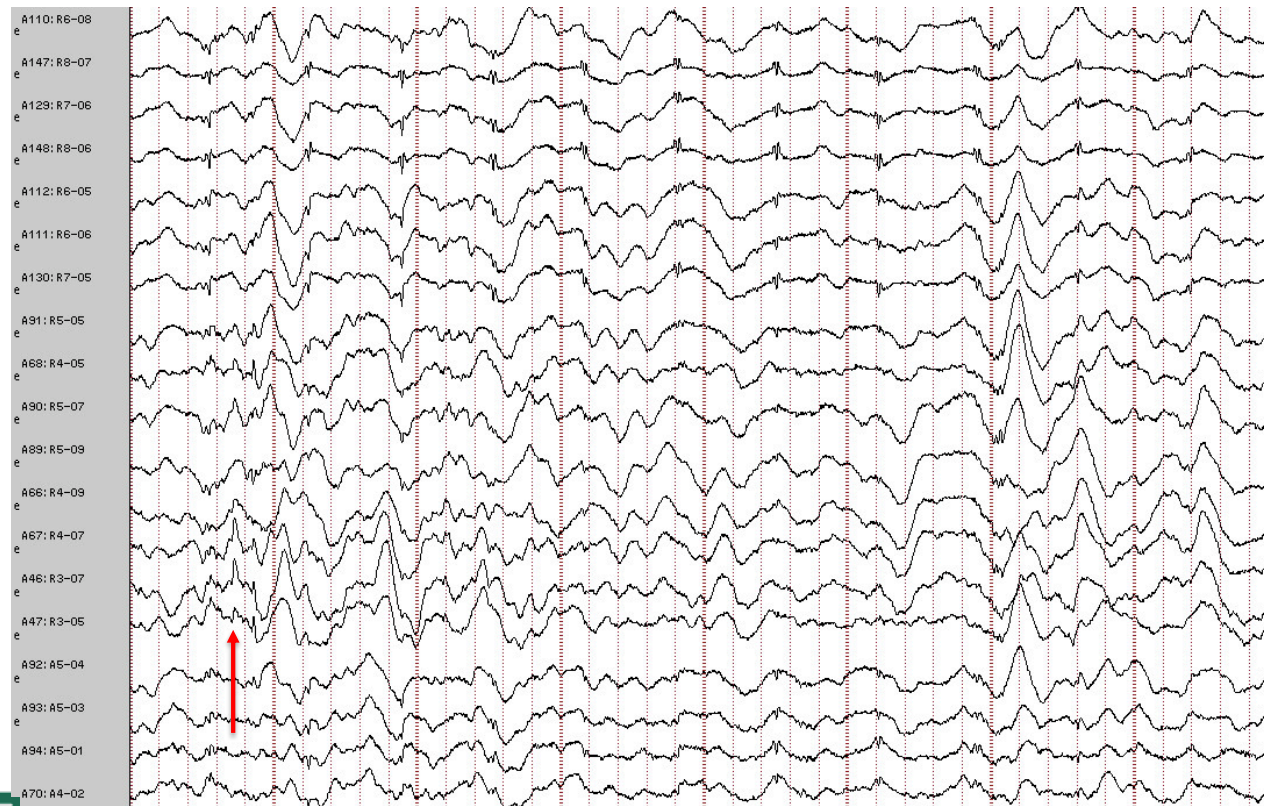


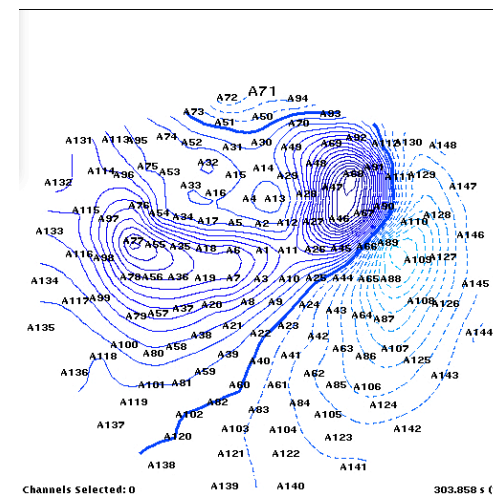
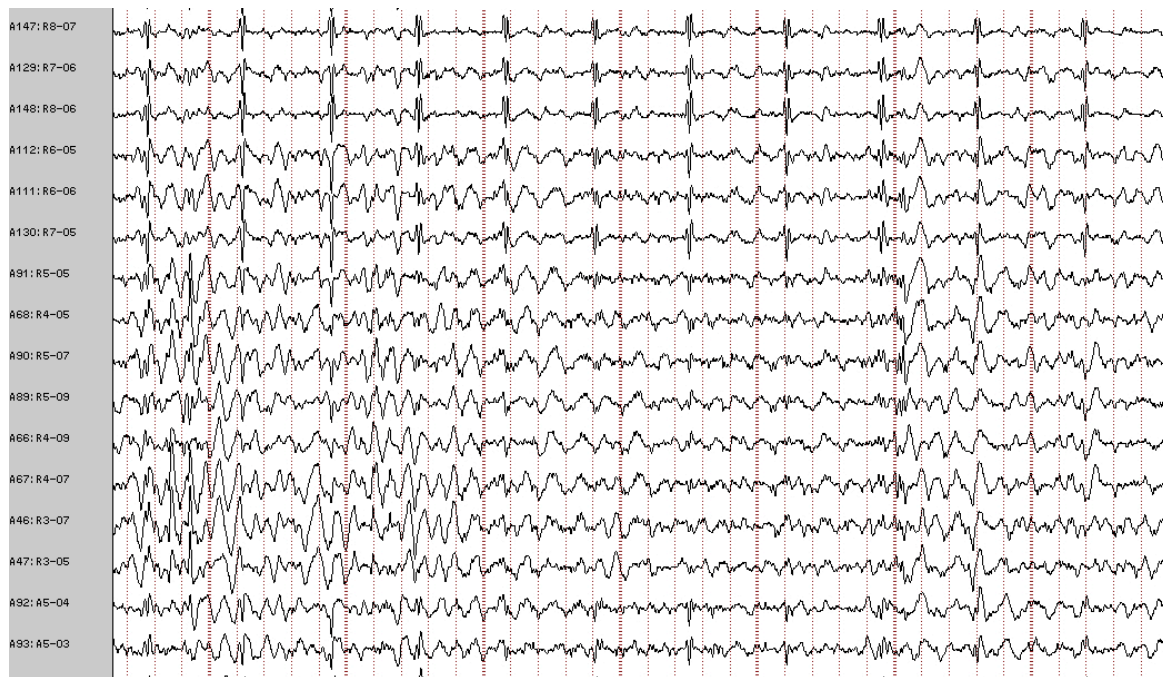


- For Epilepsy data: the simplest approach is the rejection of epochs containing cardiac QRS waves.
- For evoked responses: Consider rejecting trials with a huge QRS complex

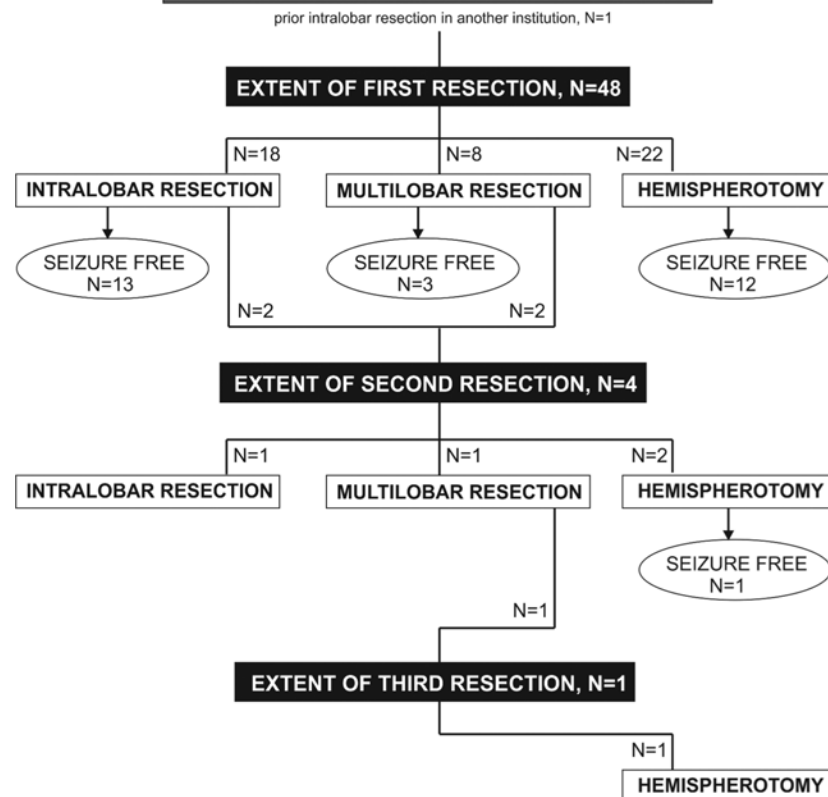


- Background is slow and of high voltage

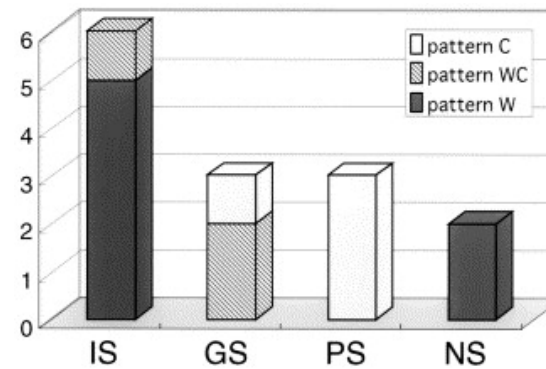
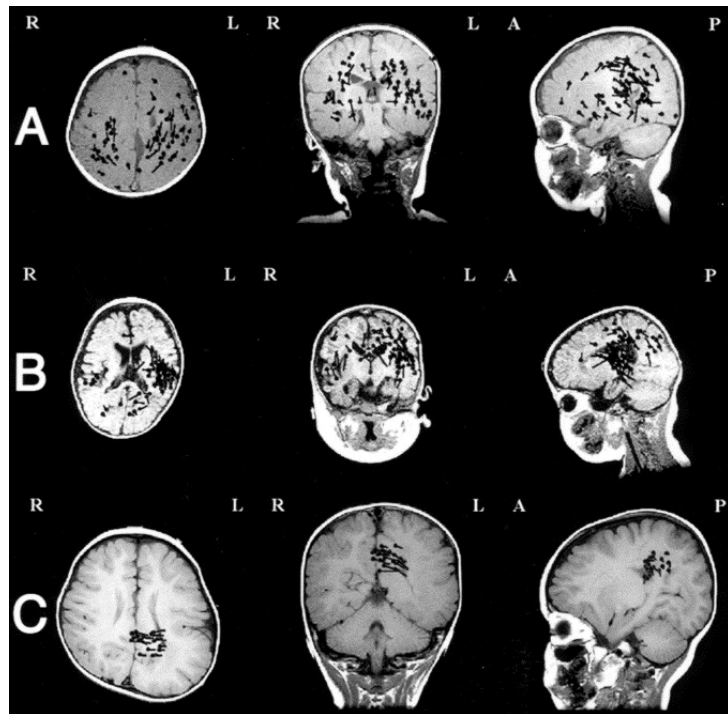




EPILEPSY SURGERY IN CHILDREN <3 YEARS

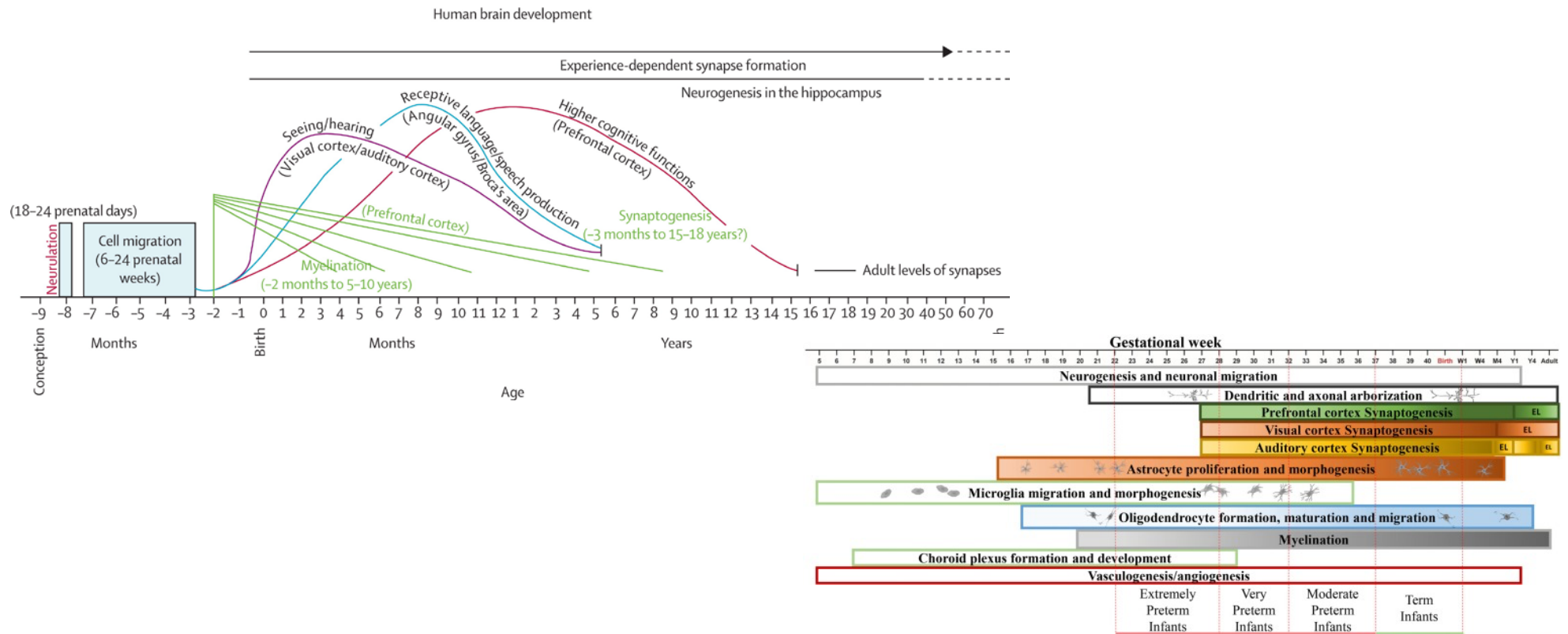


- More frequent multifocal discharges and secondary bilateral synchrony

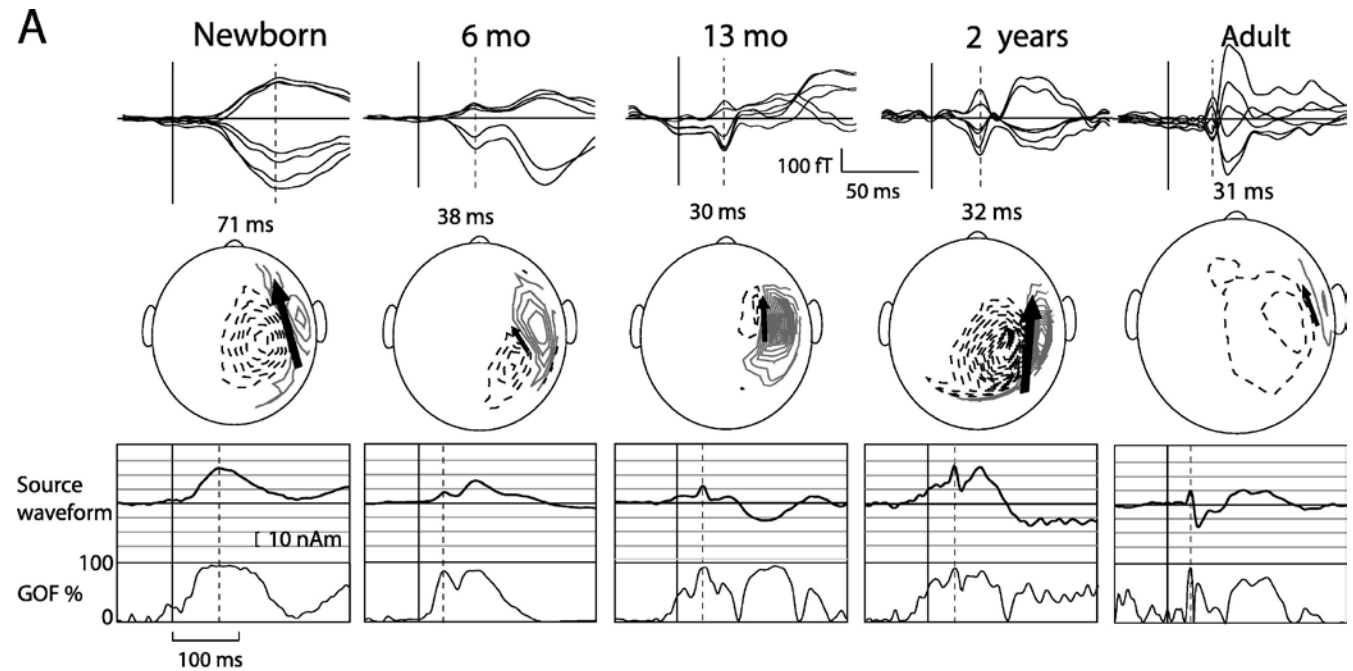
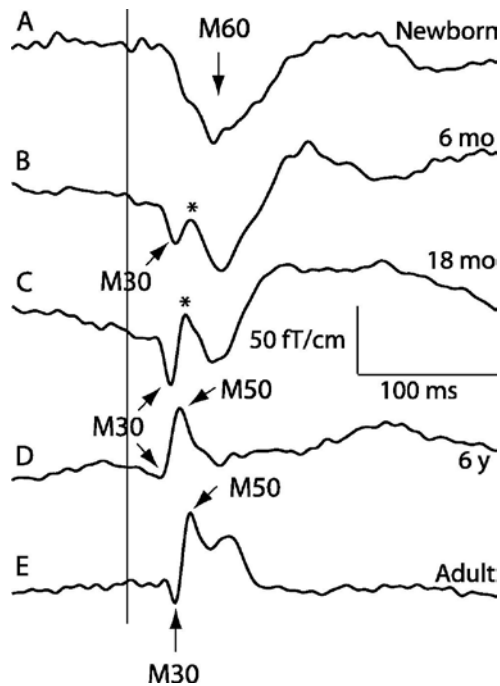


Hattori et al., Brain & Development 2001

Developmental Challenges

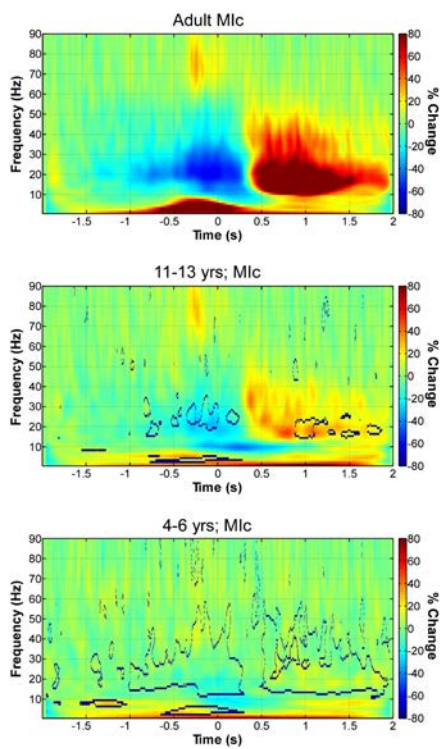


Somatosensory Evoked Responses

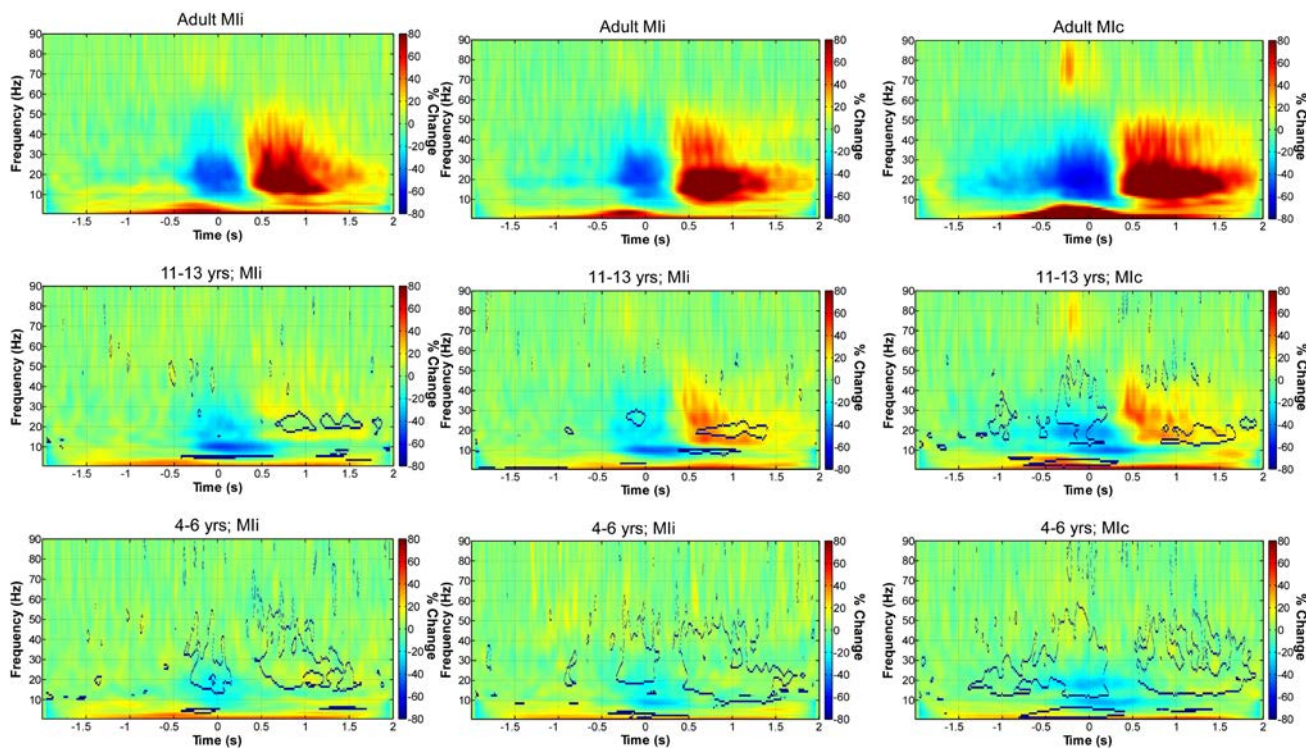


Motor Oscillations

a Group Average TFRs: Right Finger Movement



b Group Average TFRs: Left Finger Movement



Functional Mapping

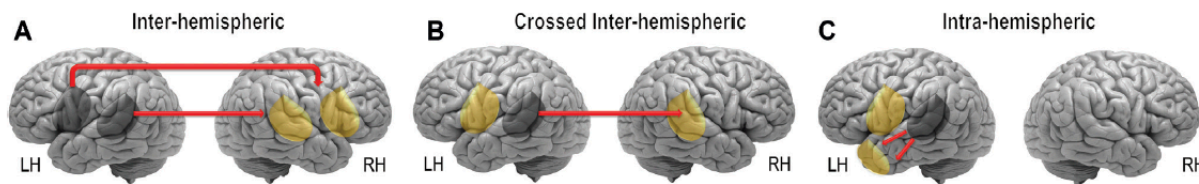
- Factors affecting reorganization after an early life insult
 - Nature and extent of the lesion (diffuse versus focal)
 - Extent of the lesion (small, large)
 - laterality of brain damage;
 - The neural network serving the impaired skills
 - Timing of insult with respect to developmental stage of the child.

Mode of reorganization	Age at onset	Lesion characteristics
Interhemispheric transfer	Infancy	Small or large unilateral lesions, e.g. hemispherectomy
Intrahemispheric transfer	Prenatal—preschool	Unilateral, focal lesions, e.g. stroke, tumour, focal dysplasia
Intrahemispheric maintenance	Through childhood, although outcome worse at younger age	Bilateral, generalized/diffuse e.g. traumatic brain injury, hypoxic-ischaemic encephalopathy



Functional Mapping

- Mechanisms of recovery after early brain insult:
- Interhemispheric reorganization— functions transfer to the analogous site in the non-damaged hemisphere;
 - Intra-hemispheric reorganization—reorganization of functions within the damaged hemisphere
 - Intra-hemispheric maintenance—skills subsumed by damaged tissue are maintained within that tissue, resulting in maximum dysfunction



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