Spreading Cortical Depression (SCD) from Pathology: Can we detect signals non-invasively using DC-MEG?

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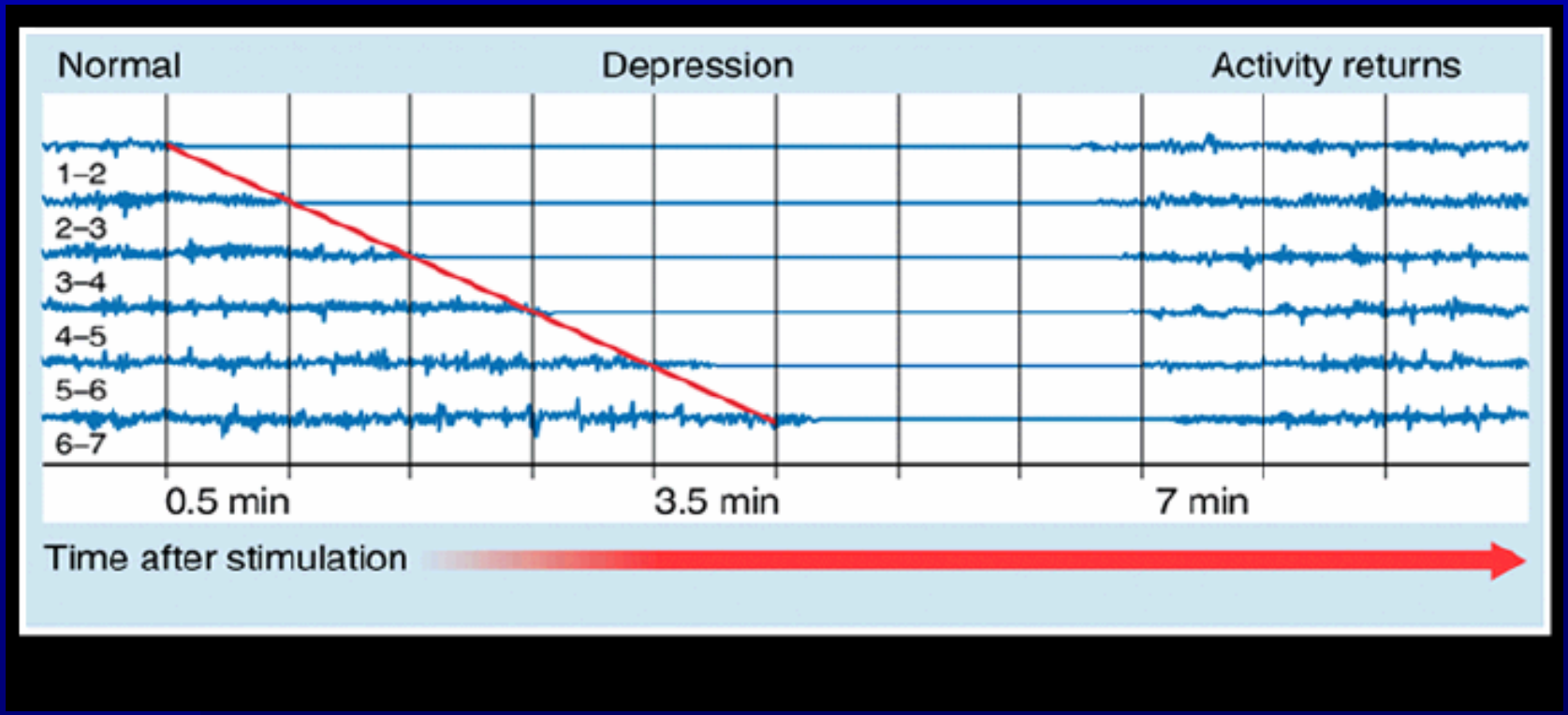
Spreading Cortical Depression

Leâo, (J. Neurophsiol 7: 379-390, 1944) first reported SCD, a disturbance of the function of neurons in the cortical environment

A region of cortical hyper-excitation is followed by suppression which propagates over cortex with a speed of 3 to 4 mm/minute.

Spreading Depression Of Leâo



Silberstein SD et al. *Headache in Clinical Practice*. 1998.

SCD Pathologies

- Epilepsy, Migraine, Anoxia, Ischemia, Head trauma
- Detection of brain activity during SCD like events has uses in the clinical evaluation of a number of these neurological disorders.

SCD

- After 60 years of studying SCD
  the biophysics are still incomplete

- What is known:
  all-or–none process
  rising extracellular $[K^+]_o$ concentrations
  and/or glutamate can initiate SCD

SCD

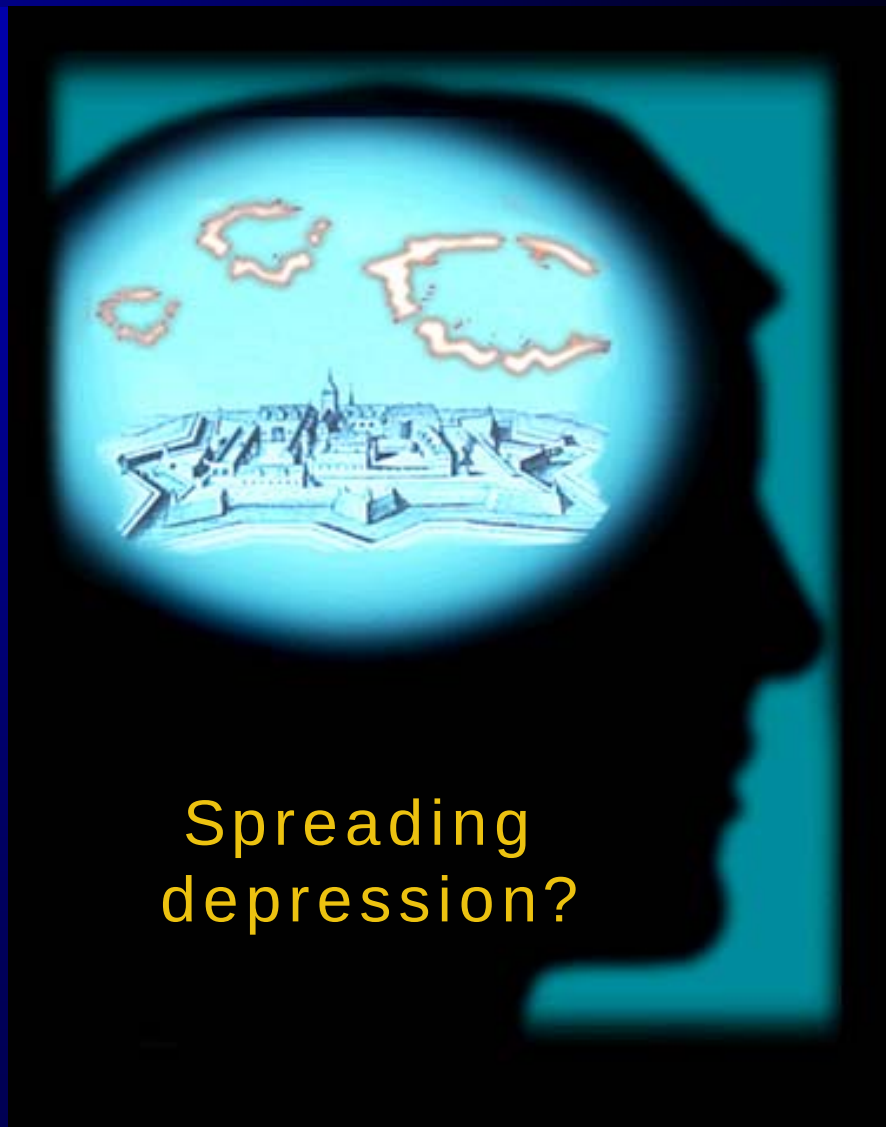
- Initiated
  - Chemical-KCl, Glutamate
  - Mechanical-pinprick or tap
  - Electrical- microamps
- Neurons
  - Vigorously discharge
  - followed by electrical inactivity
  - for several minutes
- SCD is refractory for 10 minutes or more

Membrane changes

- Potassium (K) flows out of the cell increased $[K^+]_o$ by 10 times its normal amount (3mM to 30 mM)
- Chloride (Cl) flows into the cell, decreasing $[Cl^-]_o$ by 1/2 of its normal amount (120mM to 60mM)
- Sodium (Na) flows out of the cell decreasing $[Na^+]_o$ by 1/3 of its normal amount (150mM to 50mM),
- Calcium (Ca), $[Ca^{2+}]_o$ decreased by 1/10 its normal amount (1.2mM to 0.1mM).
- water (H_20) flows into the cell
- These ionic movements cause a depolarization of the neuron.
- In the extracellular space PH levels decreased from 7.3 to approximately 6.9.

Migraine Pathophysiology the Link to SCD

The speed of SCD was identical to that deduced by Lashley (Arch Neurol Psych 46: 333-339, 1941) for the scotoma of classic migraine, suggesting that SCD is involved in migraine.



Migraine

- Migraine affects 23 million Americans
- It is characterized by intense, recurring pain on one or both sides of the head and is usually accompanied by nausea, vomiting, and increased sensitivity to light.
- The Henry Ford Hospital MEG lab, in Detroit, has studied migraine since 1988.

MEG Studies of Migraine-1

- Welch suggested MEG could detect SCD during migraine (Arch Neurol, 44: 323-327, 1987).
- Okada et al detected magnetic fields due to SCD in turtle cerebellum

  (Brain Res. 442:185-190, 1988).
- Barkley et al detected MEG fields of SCD during human migraine, demonstrating the DC MEG shift and suppression of spontaneous activity

  (Headache 30: 428-434, 1990).

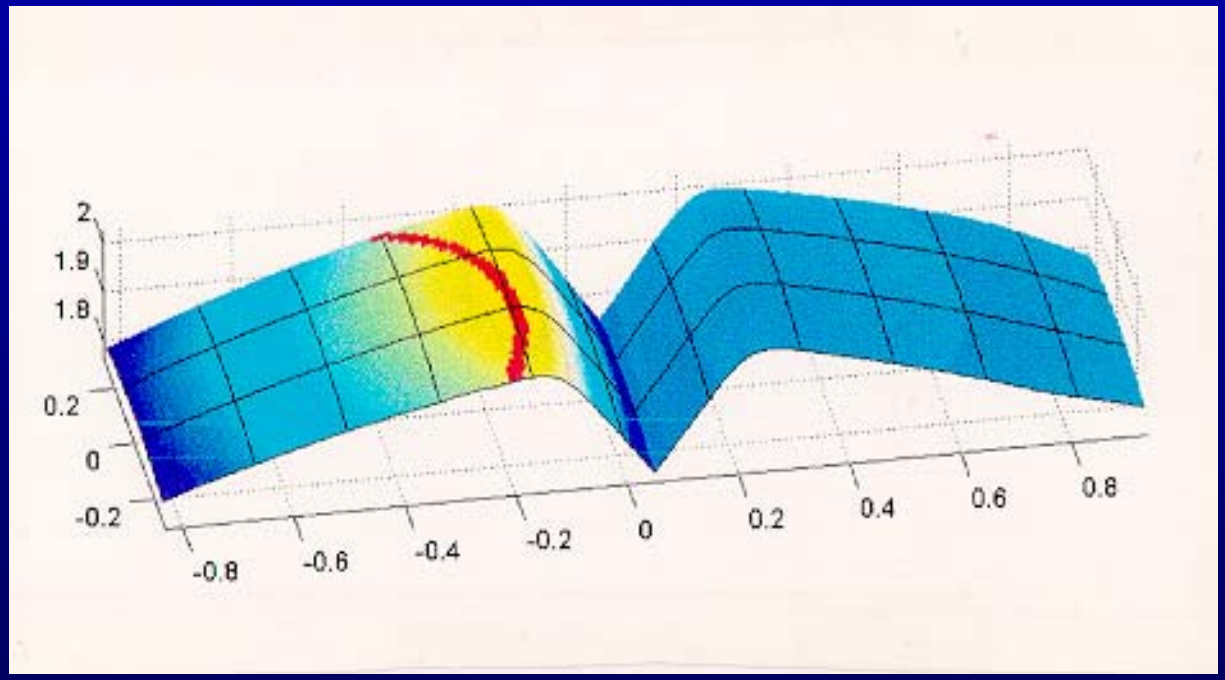
MEG Studies of Migraine-2

- Gardner-Medwin with the HFH group observed MEG fields from a rabbit model

  (Brain Res. 540:153-158, 1991).
- Bowyer et al measured MEG fields from SCD in rabbit and swine models

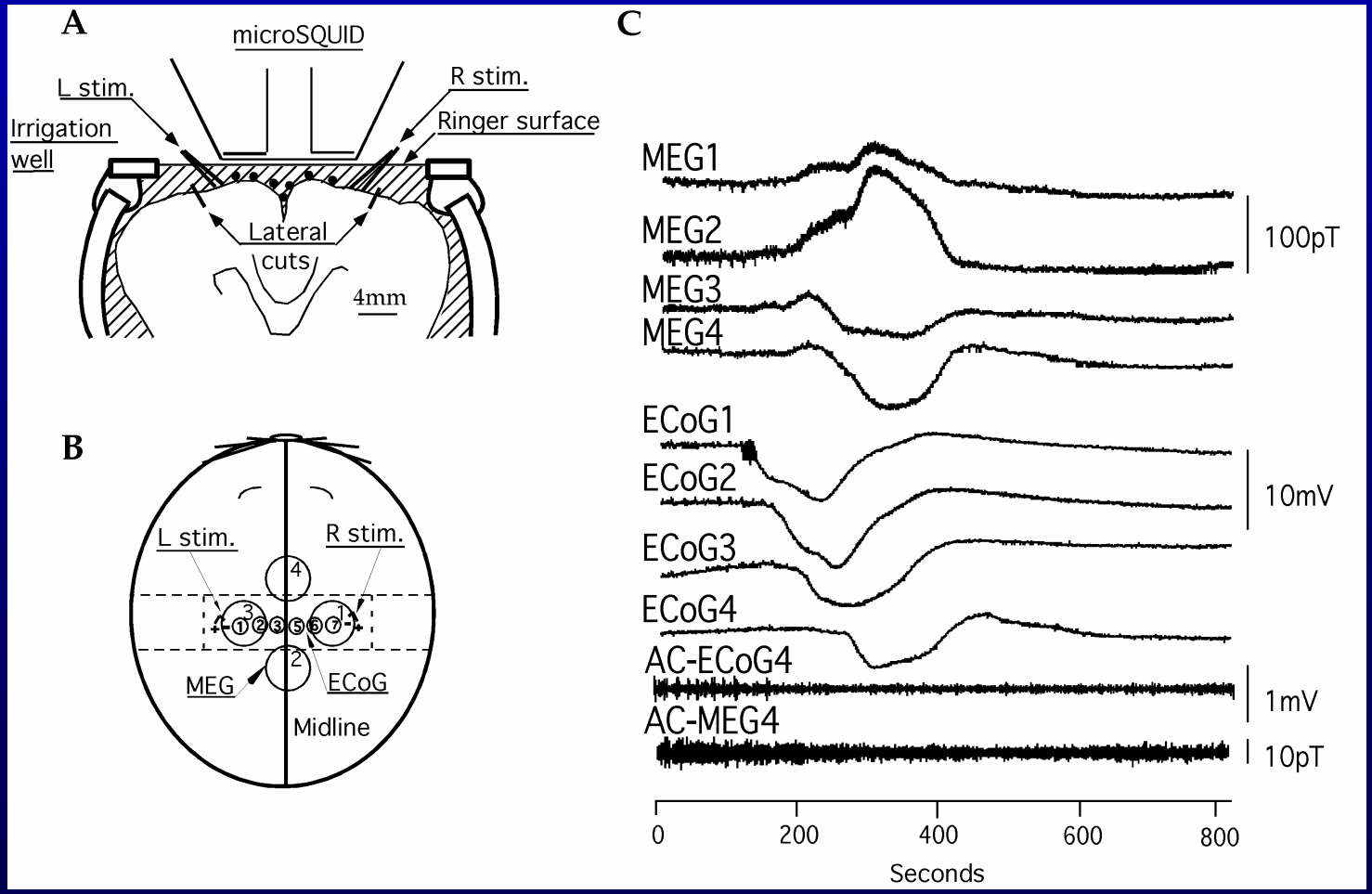
  (Brain Res. 843: 71-86, 1999).
- Such Animal Model studies validated our measurements of MEG fields in human migraine.

Spreading Cortical Depression (SCD) cortical model

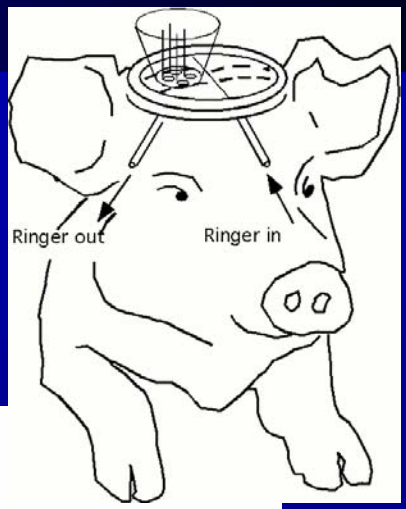


Spreading Cortical Depression (SCD) on Lissencephalic cortex (rabbit model)

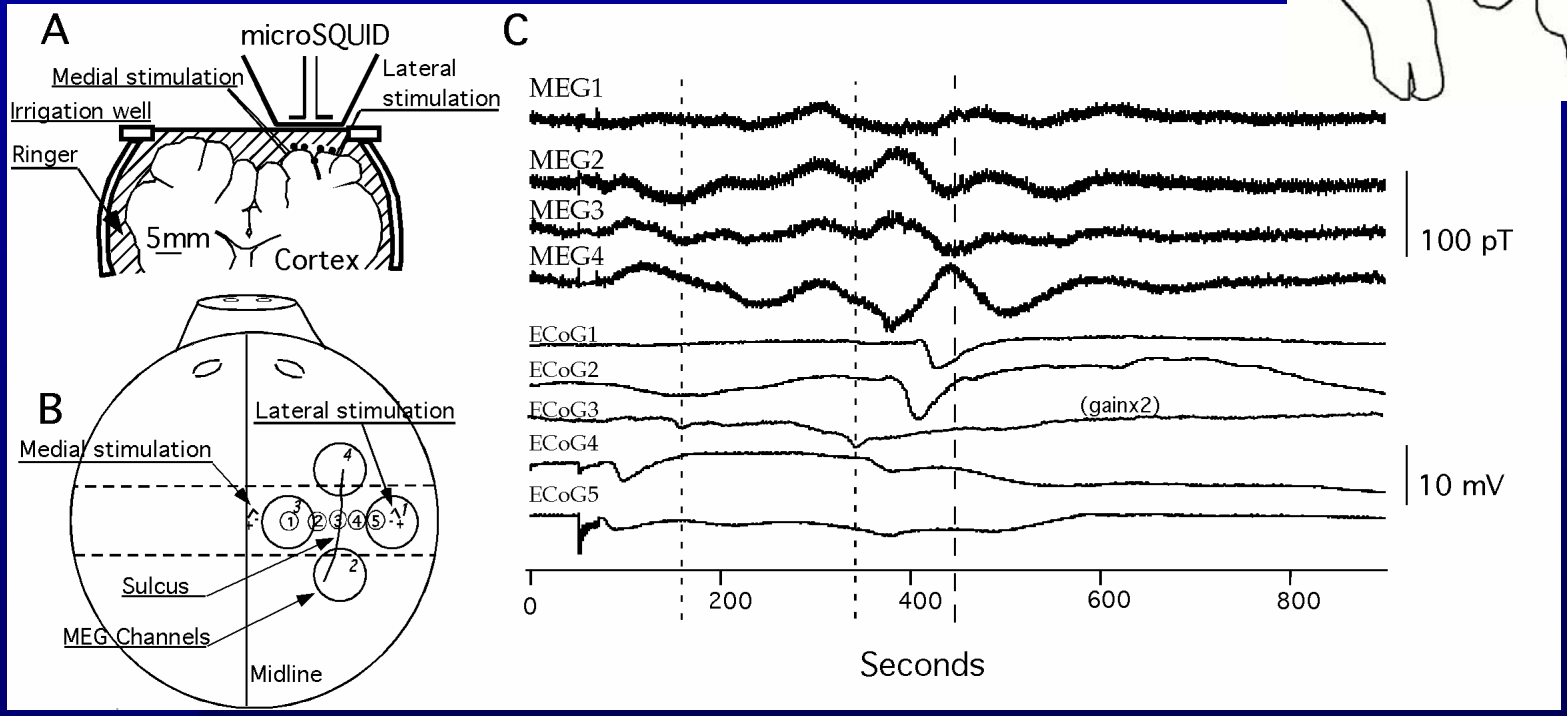
Brain Research 843:66-78, 1999



Spreading Cortical Depression (SCD) on Gyrencephalic cortex (swine model)



Brain Research 843:79-86, 1999

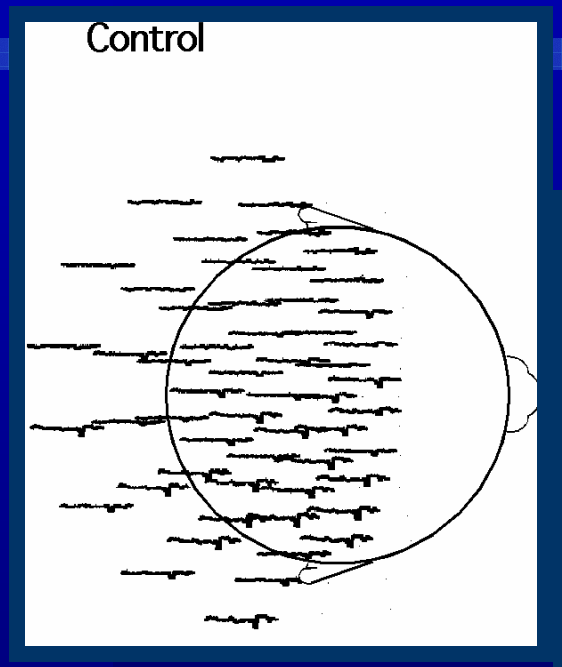


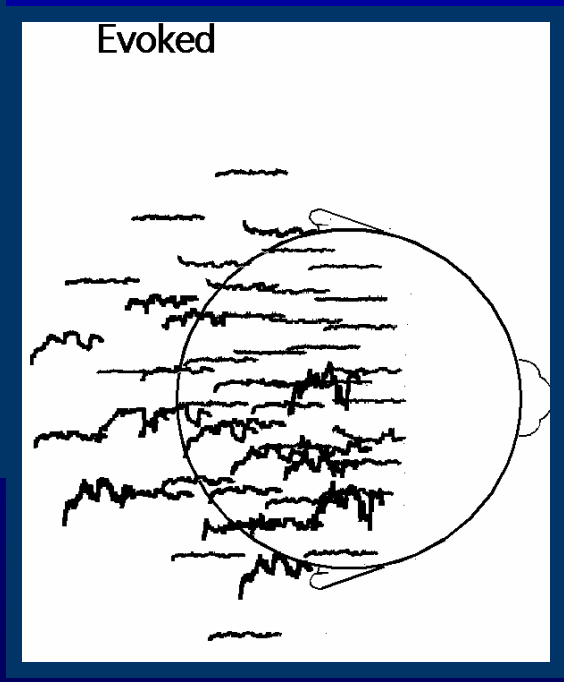
MEG Studies of Migraine-3

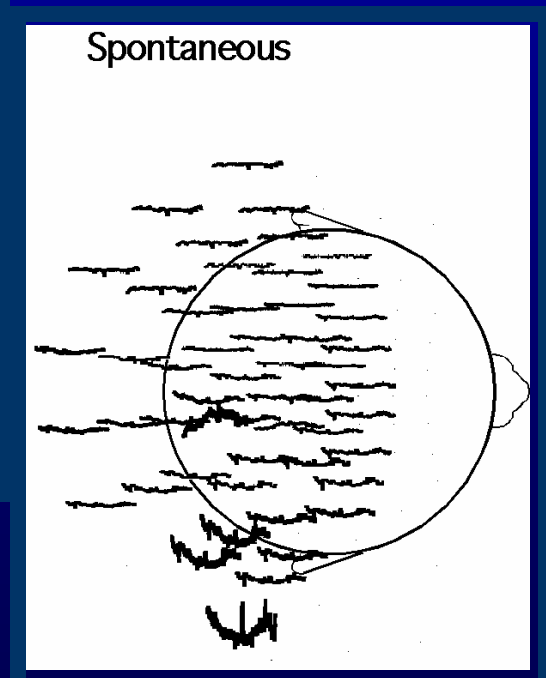
Bowyer et al used whole-head MEG (4D Neuroimaging WH 2500 Magnes) and 2DII to study spontaneous and induced Migraine, and demonstrated extent of cortical activation.

(Ann Neurol 50: 582-587, 2001)

DC-MEG Waveforms



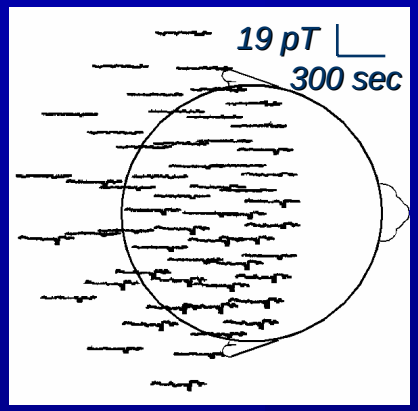




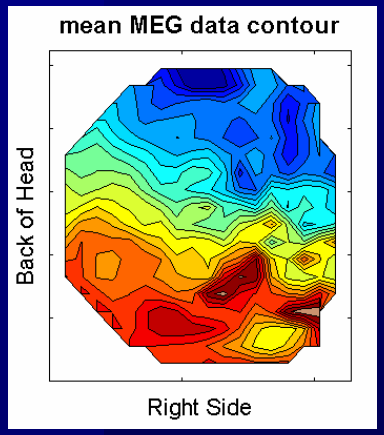
19 pTesla

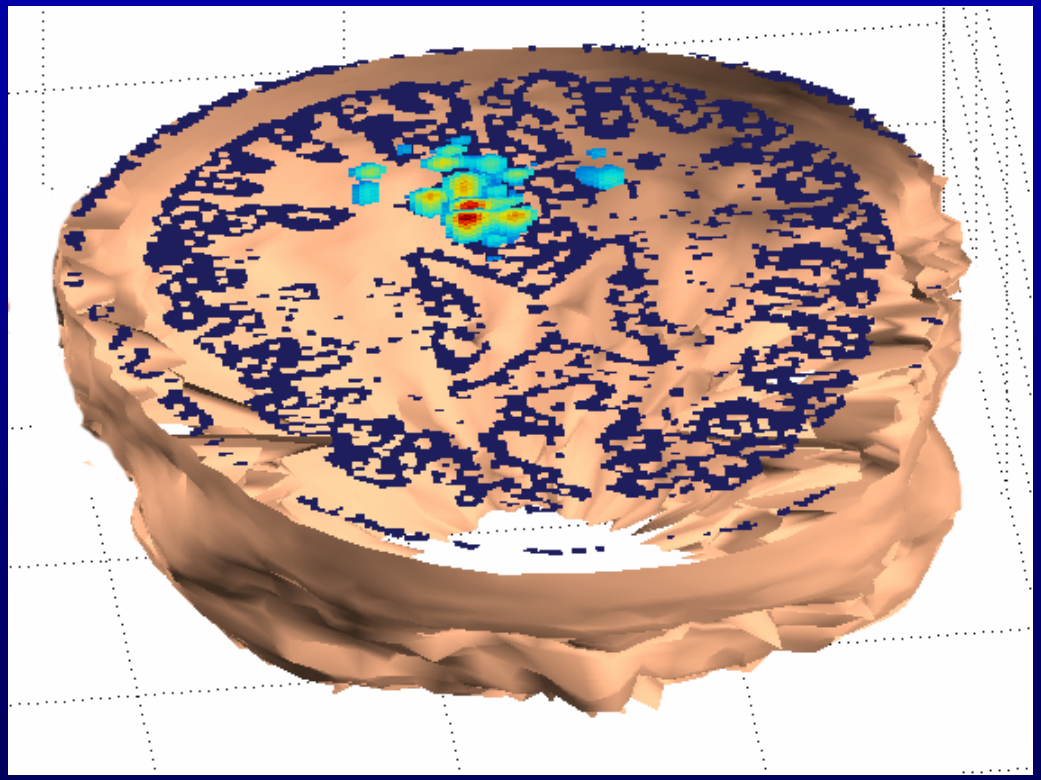
300 seconds

Control Subject



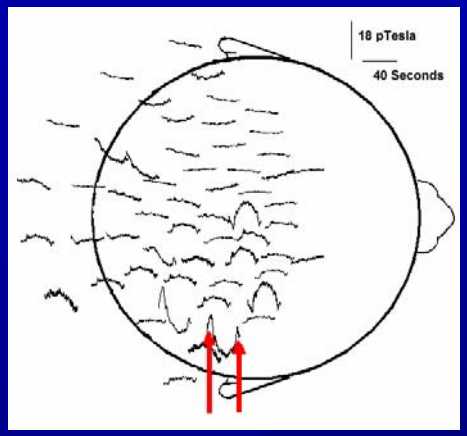
MEG data



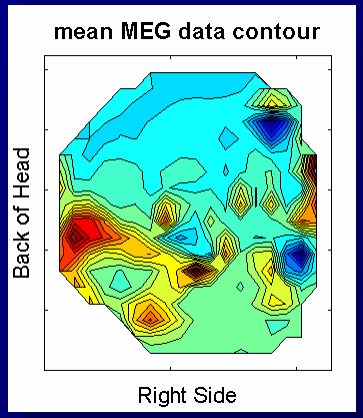


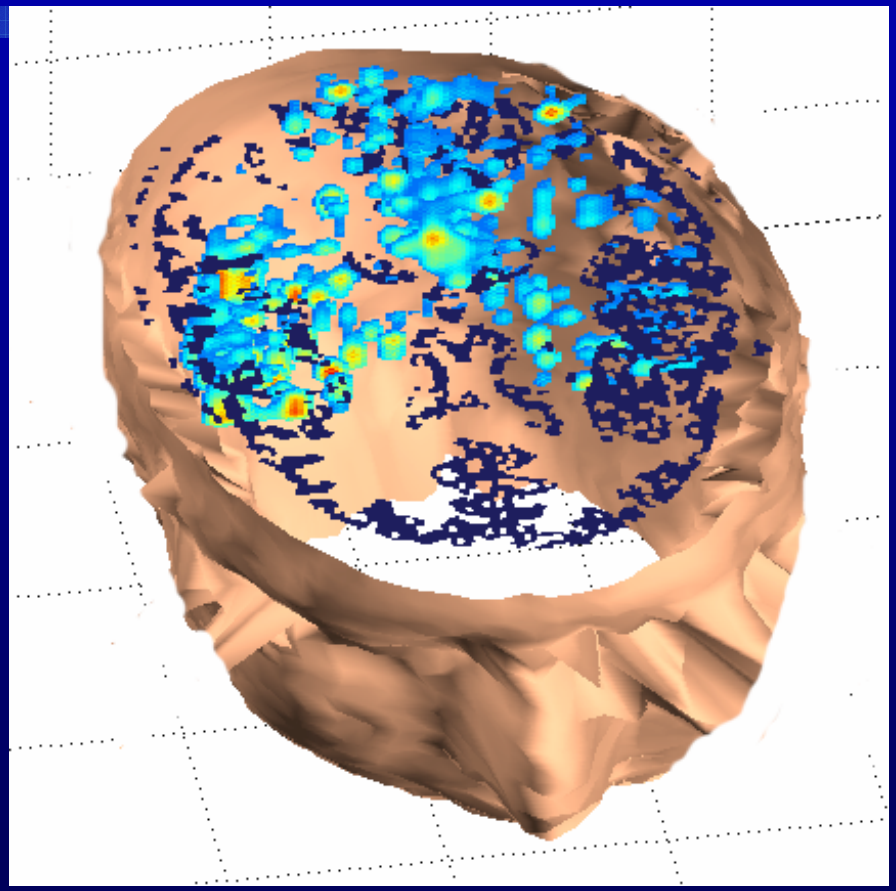
Mean cortical source amplitudes

Evoked Migraine Subject



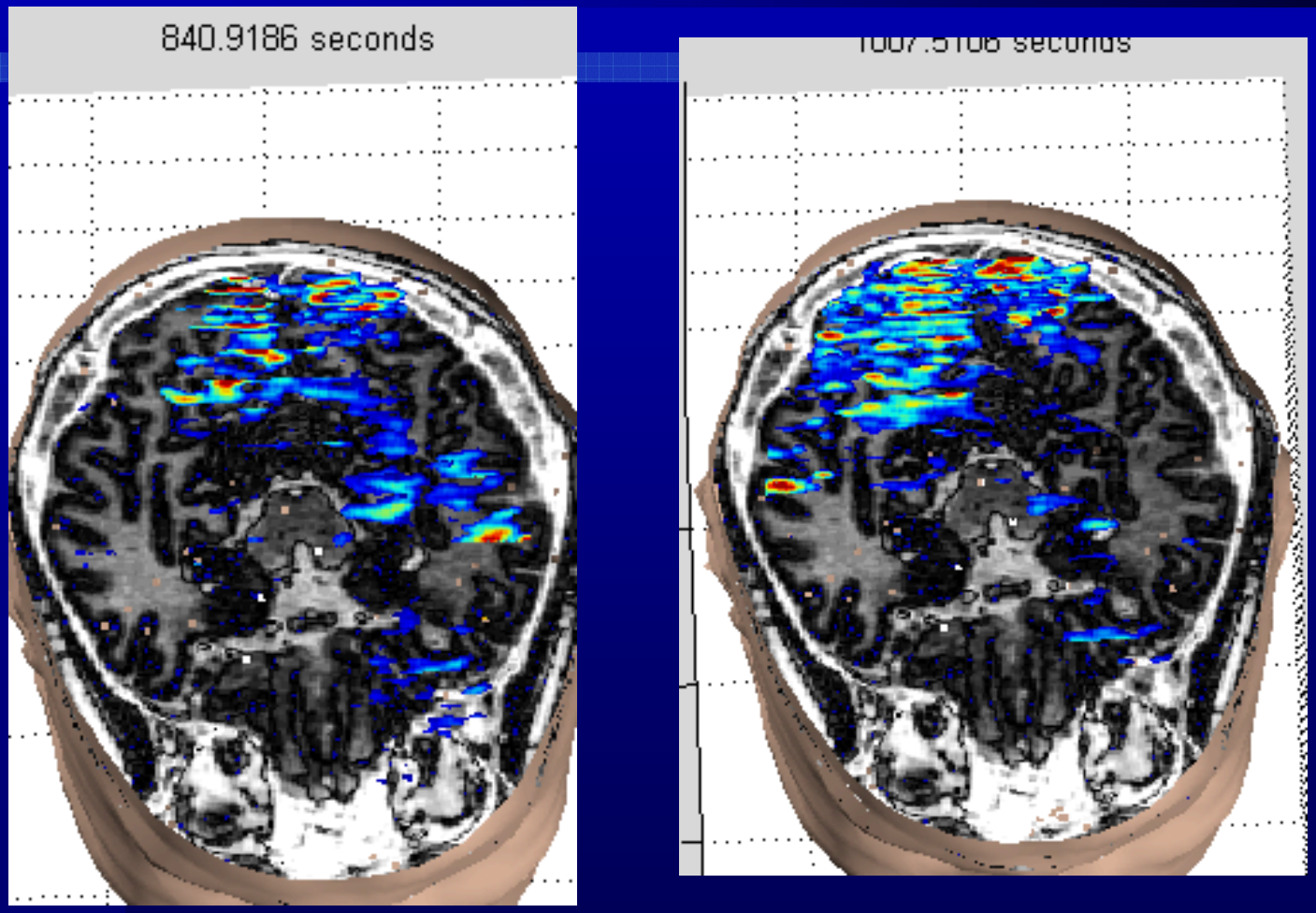
MEG data



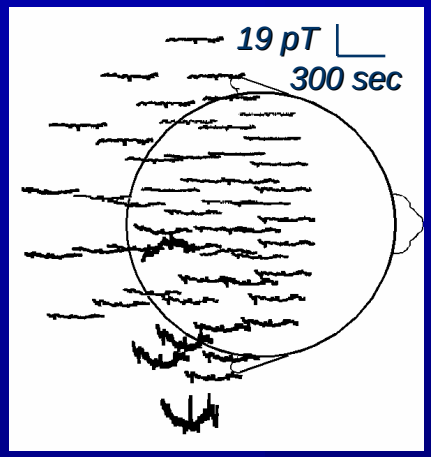


Mean cortical source amplitudes

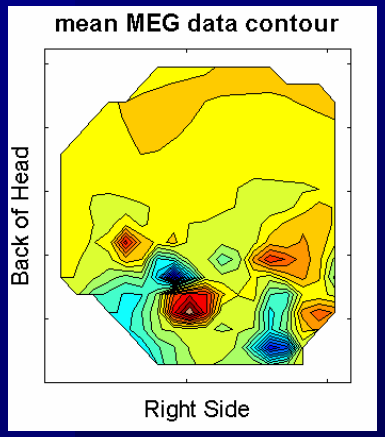
Evoked Migraine Subject

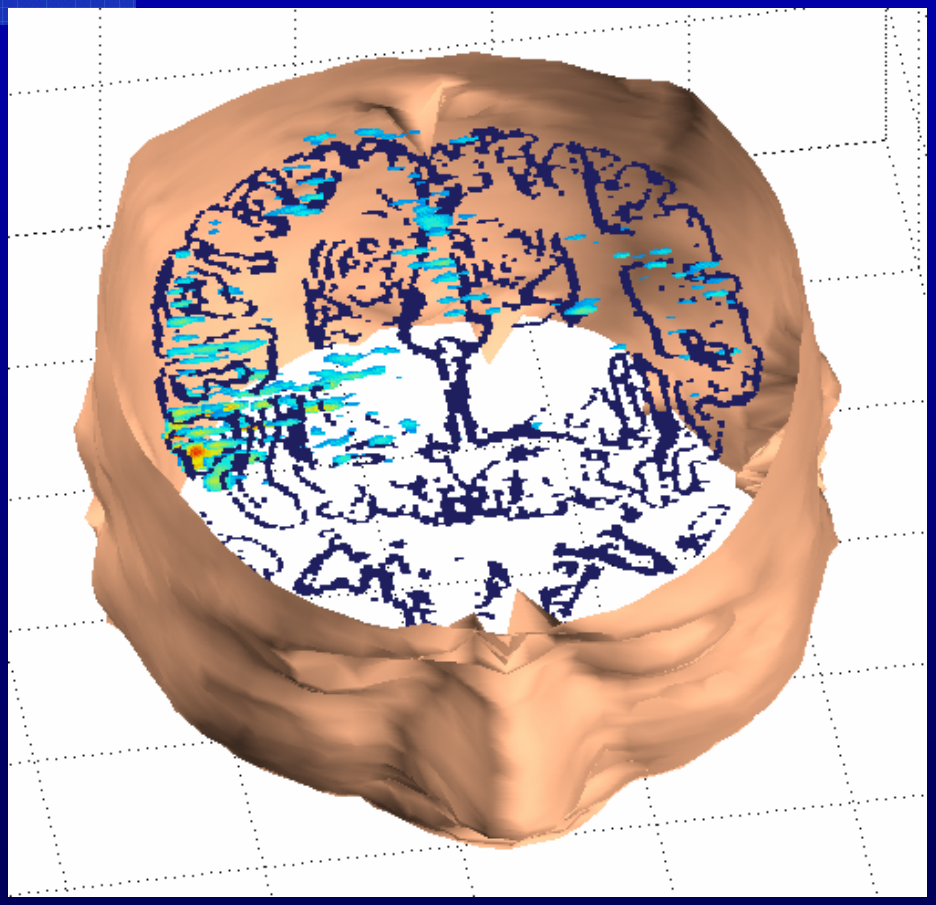


Spontaneous Migraine Subject



MEG data





Mean cortical source amplitudes

Results of spontaneous and induced migraine study

- 8 evoked and 5 spontaneous Migraines with Aura subjects:

  DC-MEG shifts of 37 $\pm$ 17 pTesla

- 6 Control subjects:

  DC-MEG shifts of less than 9 pTesla

  ($p < 0.003$ Fisher exact test)

Summary of spontaneous and induced aura study

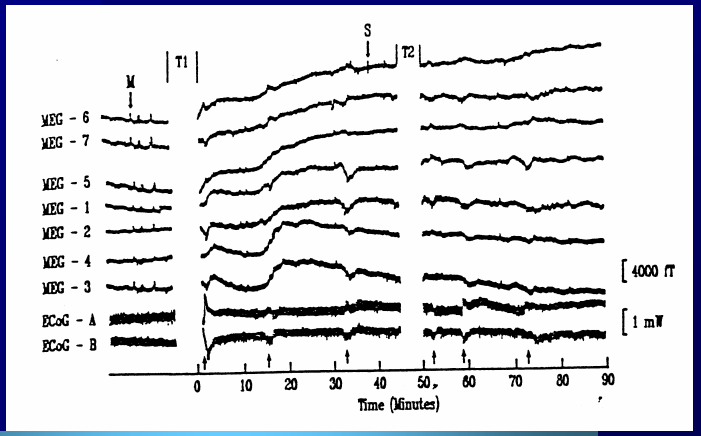
- DC Shifts during spontaneous and induced migraine were larger in amplitude than controls.
- DC-MEG Shifts reminiscent of SCD
- Numerous studies support SCD as the underlying mechanism in Migraine.
- Current DC-MEG studies include recording spontaneous brain activity in migraine patients pre and post prophylactic drug treatment.

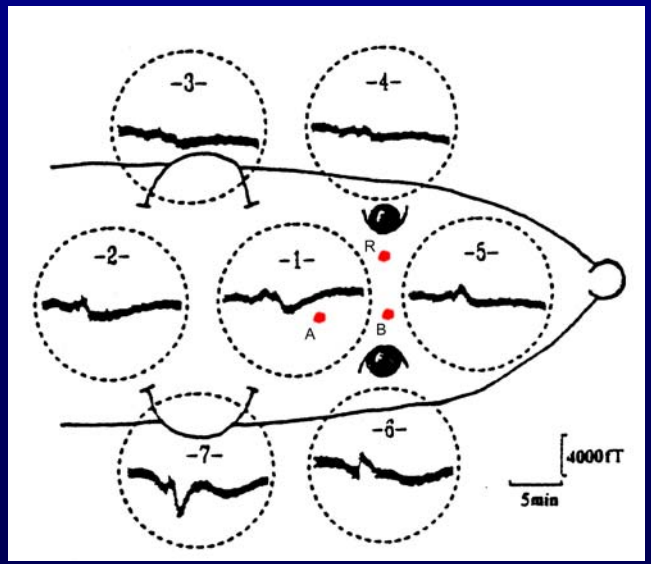
SCD-like-events-1

- **Epilepsy**: slow DC-shifts are expected during seizures (Marshal, 1959; Leao, 1944) and probably the postictal state. Since MEG can record cortical DC shifts we now record all patients undergoing MEG evaluations for interictal spike analysis with a DC high pass filter.
- **Traumatic Brain Injury:** is accompanied by an increase in intracranial pressure (ICP) and in some cases by spontaneous generation of SCD, but the role of SCD in TBI is still unknown. In a rat study as ICP increased (due to increased impact) the number of SCD events also increased (Rogatsky, 2003).

SCD like events-2

- **Stroke/ischemia:** similar phenomena are associated with peri infarct depolarizations that surround and radiate from ischemic lesions (Hossman, 1996). Chen et al showed DC MEG could detect SCD during MCAo in Rat model (Stroke, 23: 1299-1303, 1992).





Conclusion

- Further studies on SCD may render a deeper understanding of the biophysics occurring during the initiation of SCD.
- This may also lead to a more complete understanding of the neurological disturbances linked to SCD.

Acknowledgment

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