

**MEG Coherence Imaging of Low frequencies:
Applications for Stroke and Migraine
&
DC shifts in spreading cortical depression**

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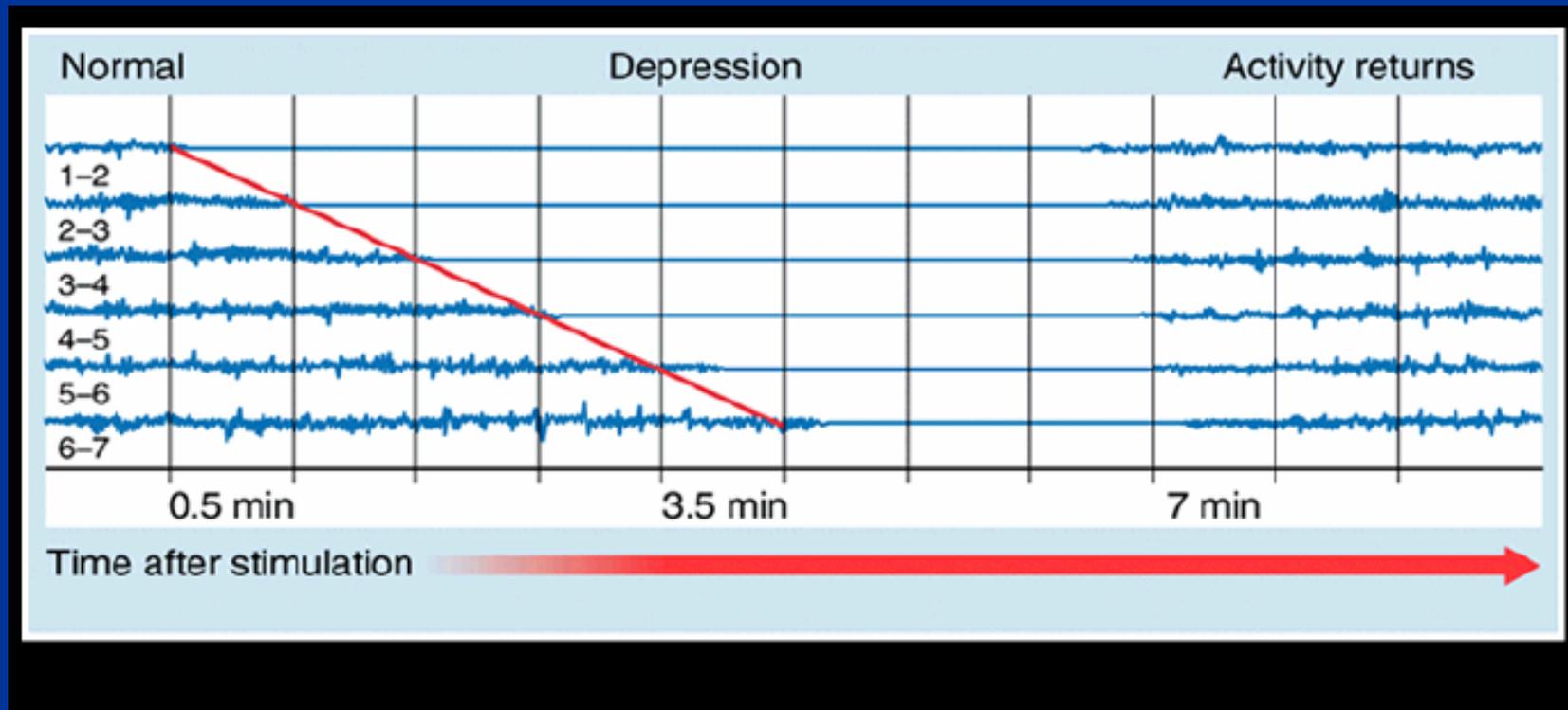


Spreading Cortical Depression

Leão, (J. Neurophysiol 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 Leão

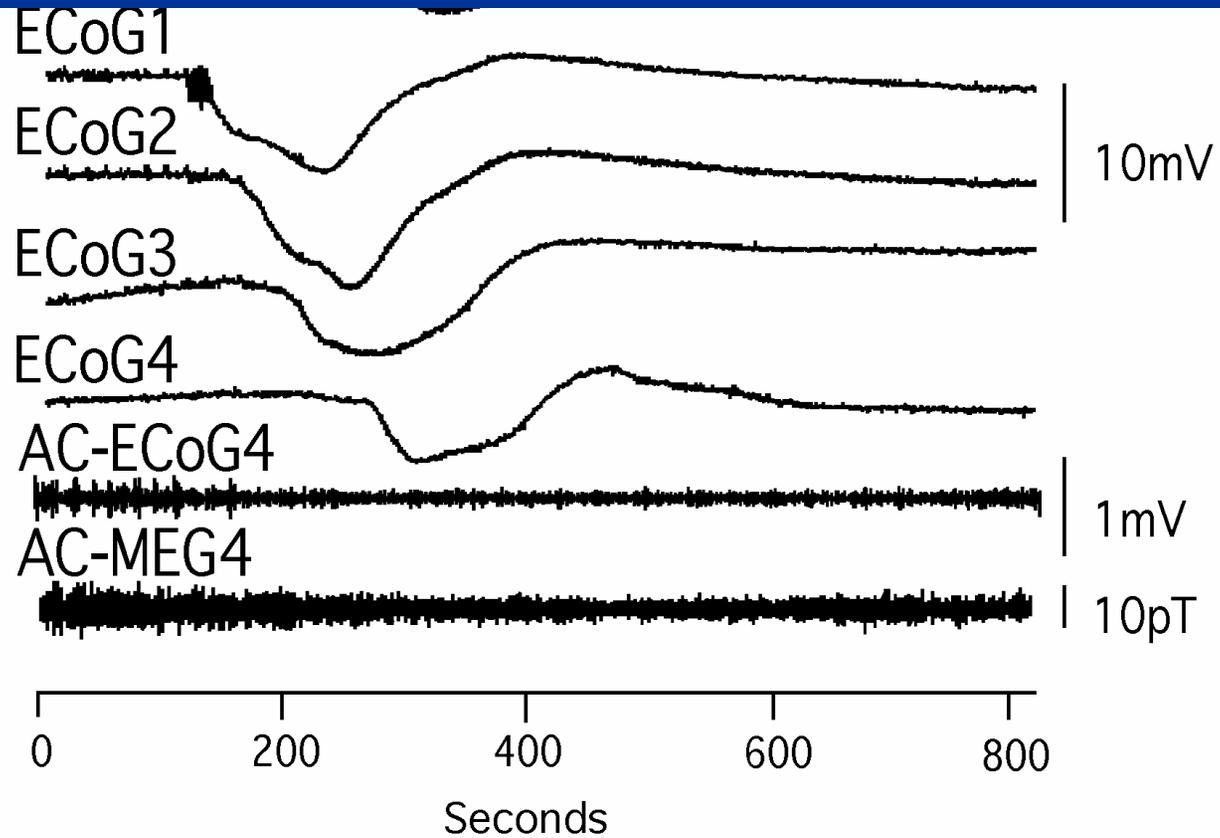
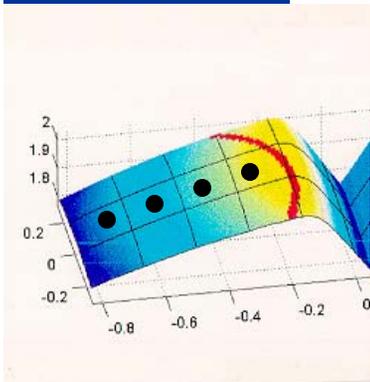


Silberstein SD et al. *Headache in Clinical Practice*. 1998.

Spreading Cortical Depression (SCD)

DC coupled Electrocorticography recording

Brain Research 843:66-78, 1999



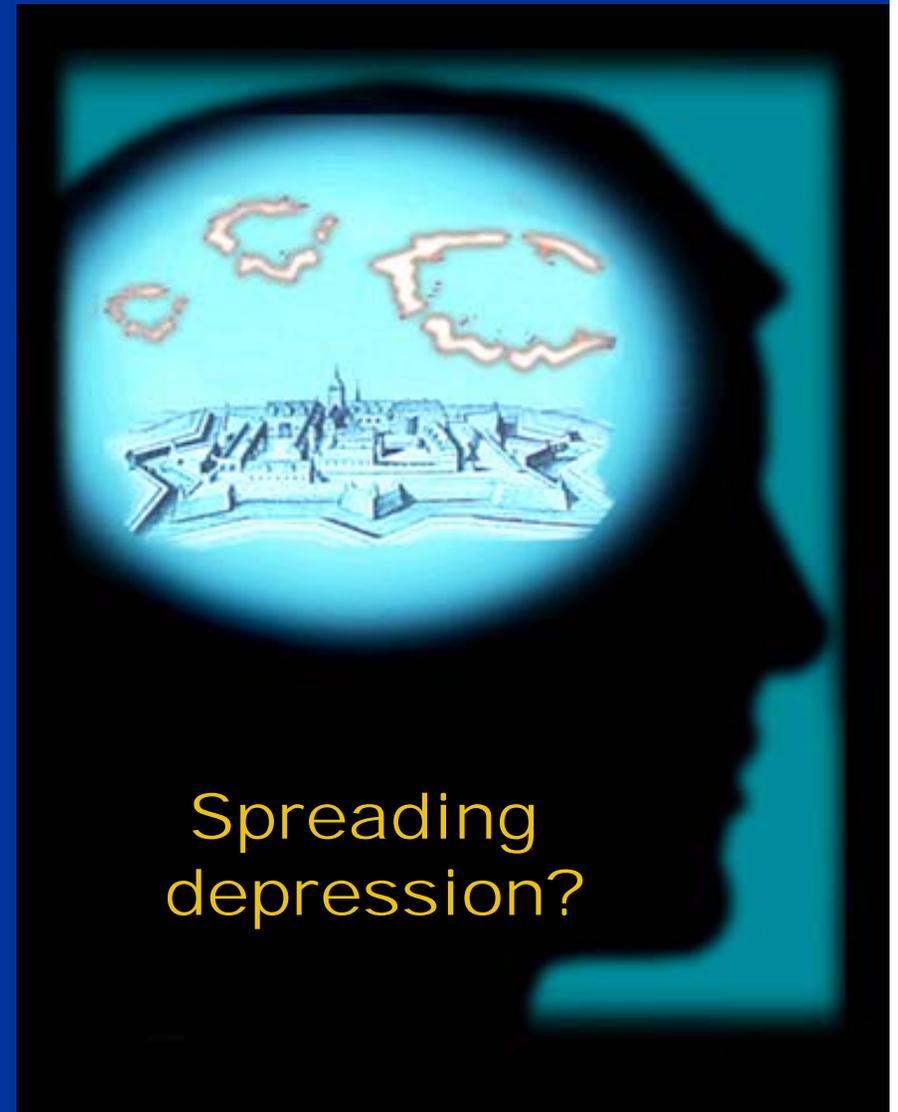
Slow Wave Brain Activity (SCD like) Linked to Pathologies

- Epilepsy (Baayen et al. 2003)
- Migraine (Barkley et al 1990)
- Brain lesion (Veith et al 1996)
- Stroke (Gallen et al 1992)
- Tumors (de Jongh et al 2001, 2002, 2003)
- Schizophrenia (Fehr 2003, Wienbruch, 2003)
- Alzheimer disease (Fernandez 2003)

Detection of brain activity during SCD like events has uses in the clinical evaluation of a number of these neurological disorders.

Migraine Pathology the link to SCD

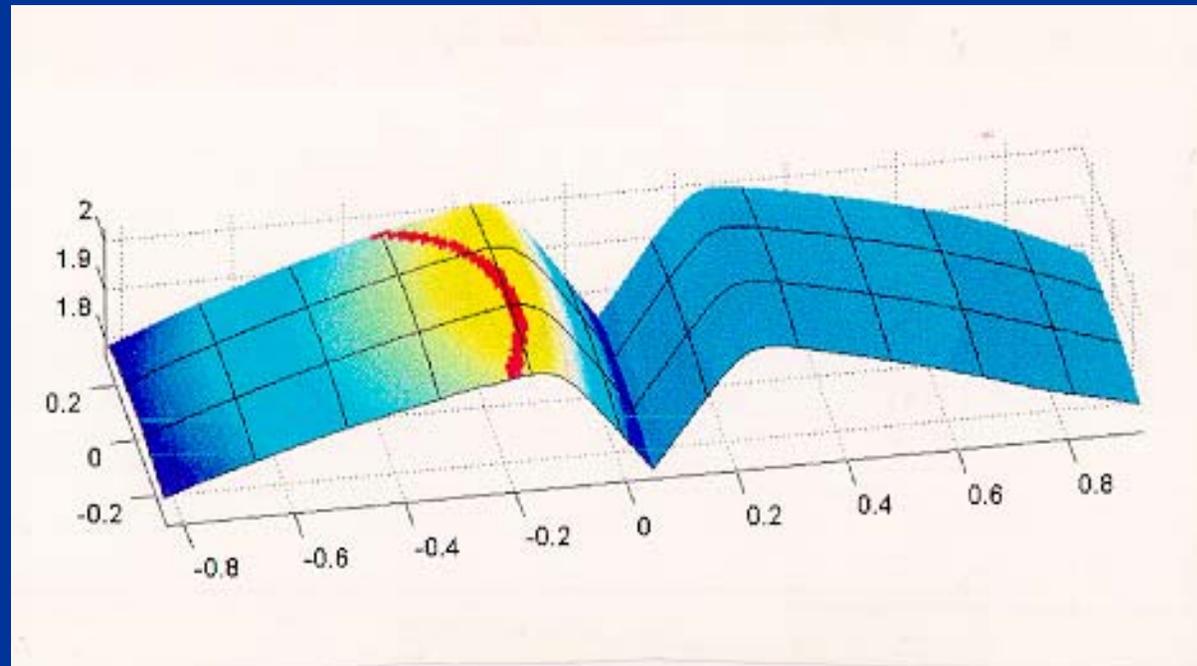
The speed of SCD was identical to that deduced by Lashley (Arch Neurol Psych 46: 333-339, 1941) for the scotoma of classic migraine, suggesting that SCD is involved in migraine.



Migraine

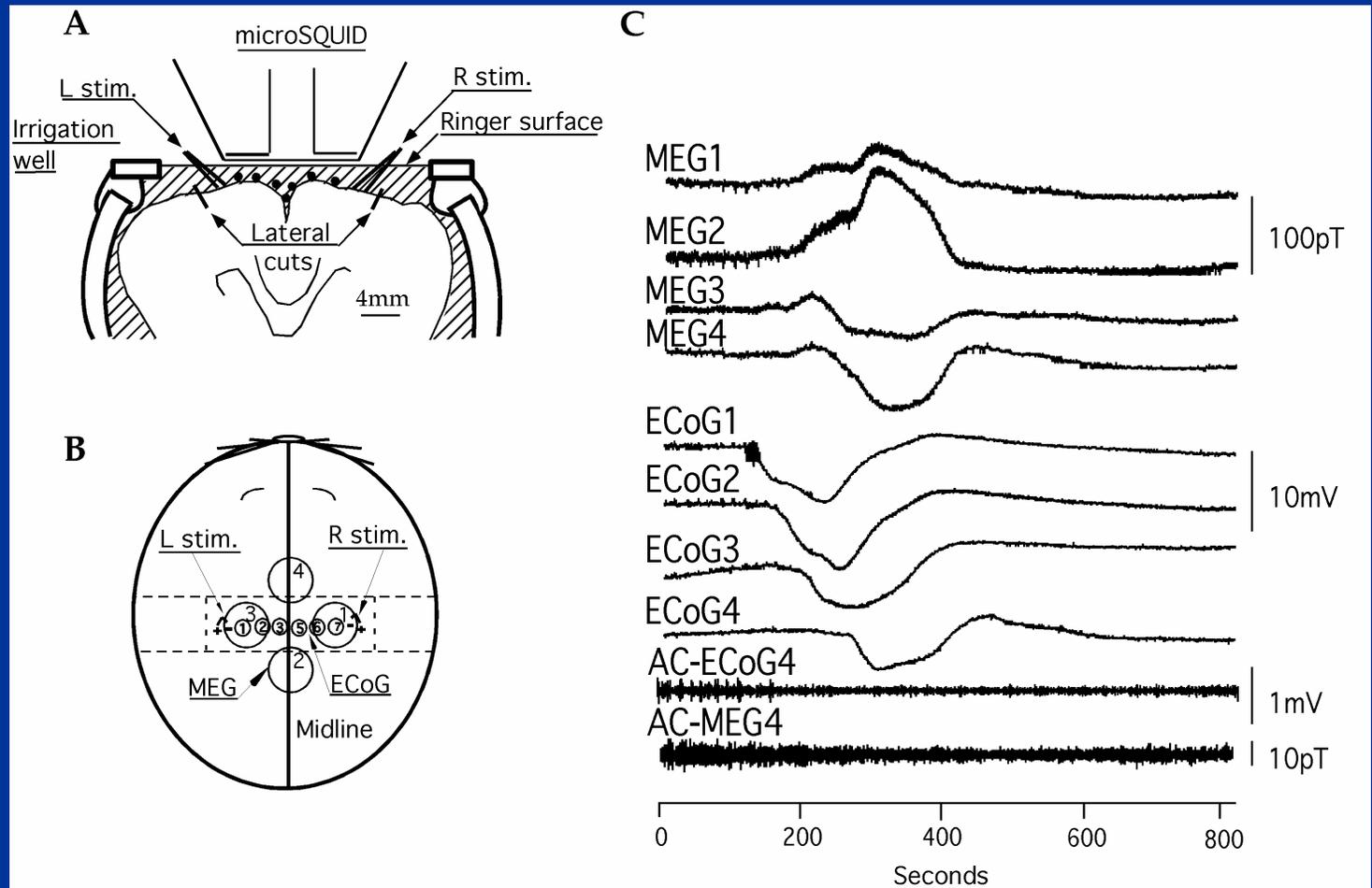
- Migraine affects 23 million Americans
- It is characterized by intense, recurring pain on one or both sides of the head and is usually accompanied by nausea, vomiting, and increased sensitivity to light.
- The Henry Ford Hospital MEG lab, in Detroit, has studied migraine since 1988.

Spreading Cortical Depression (SCD) cortical model



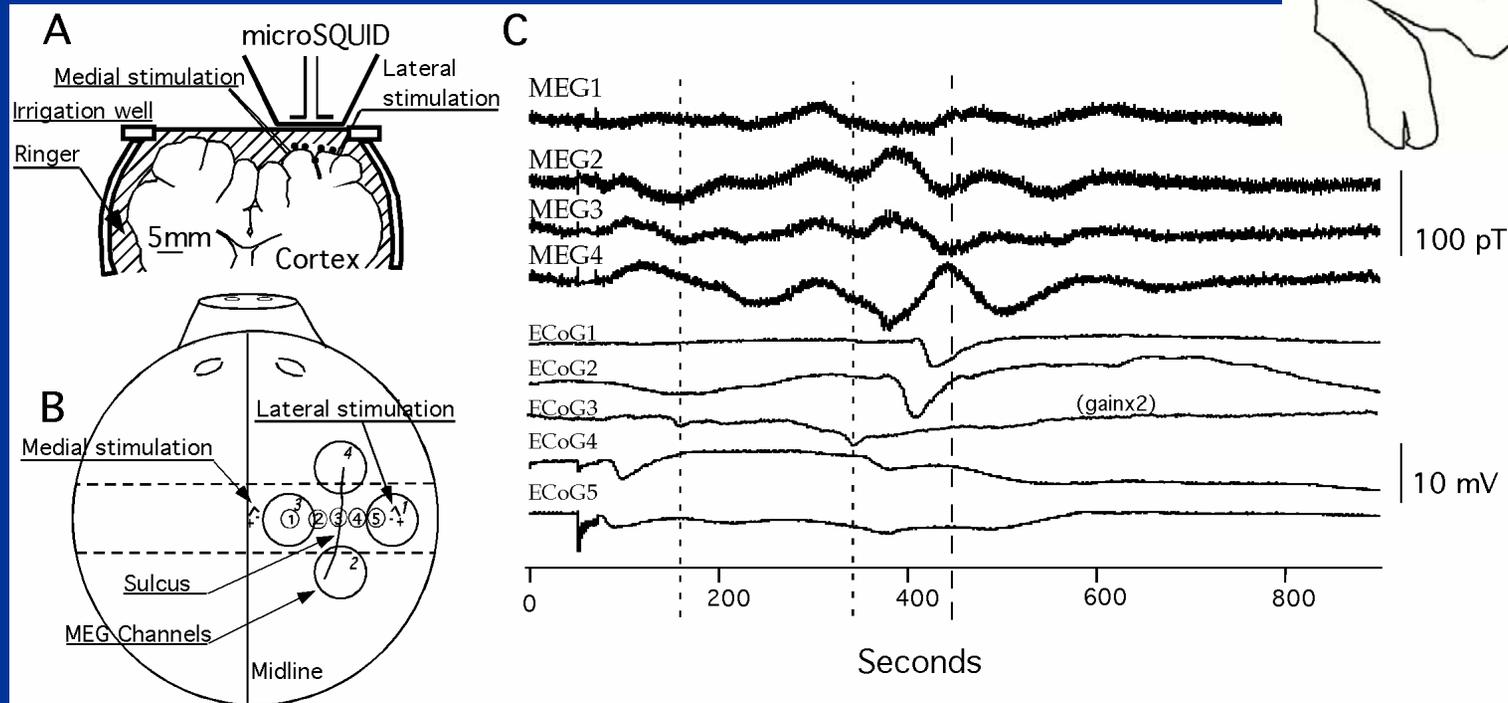
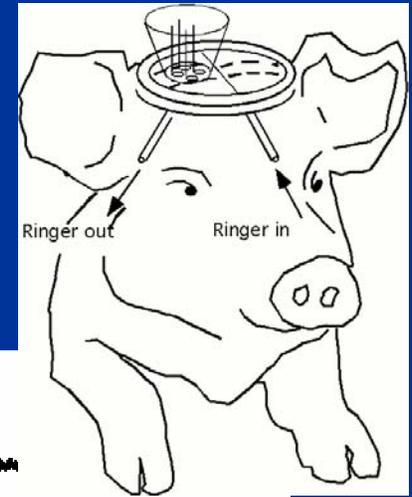
Spreading Cortical Depression (SCD) on Lissencephalic cortex (rabbit model)

Brain Research 843:66-78, 1999



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

Brain Research 843:79-86, 1999



Animal Model studies validated our measurements of MEG fields in human migraine.

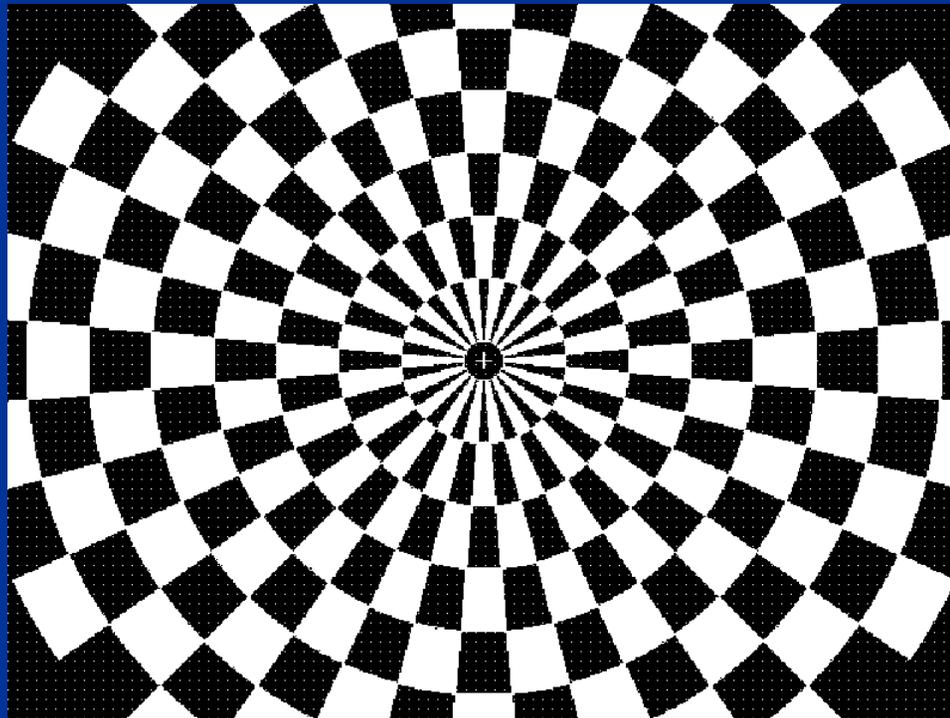
Human MEG Studies of Migraine

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)

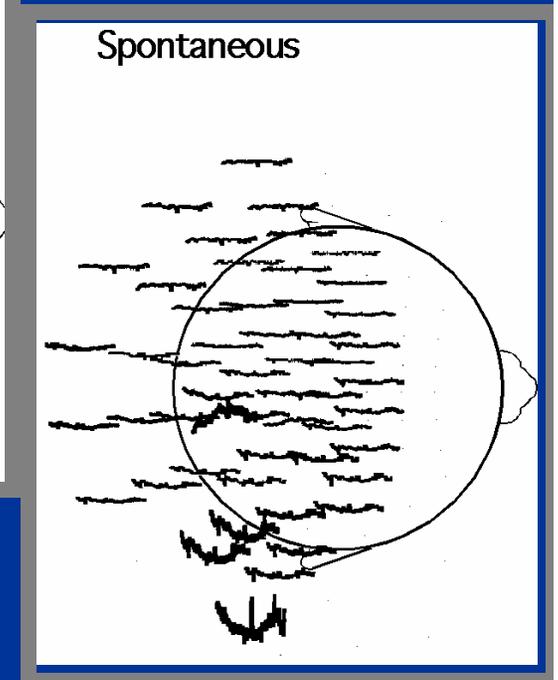
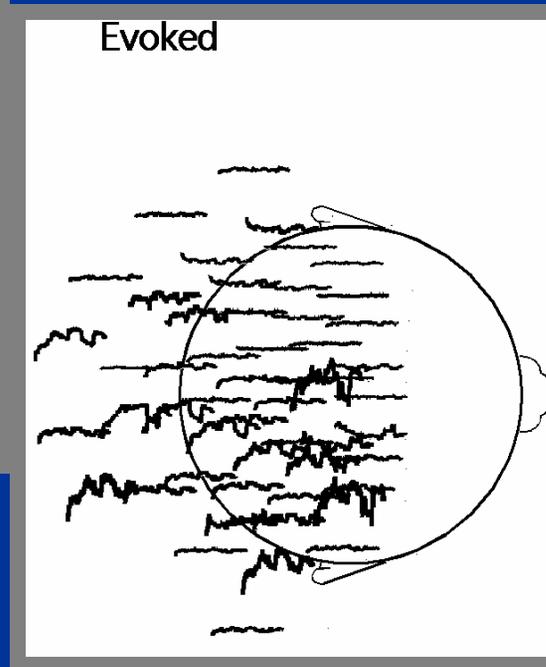
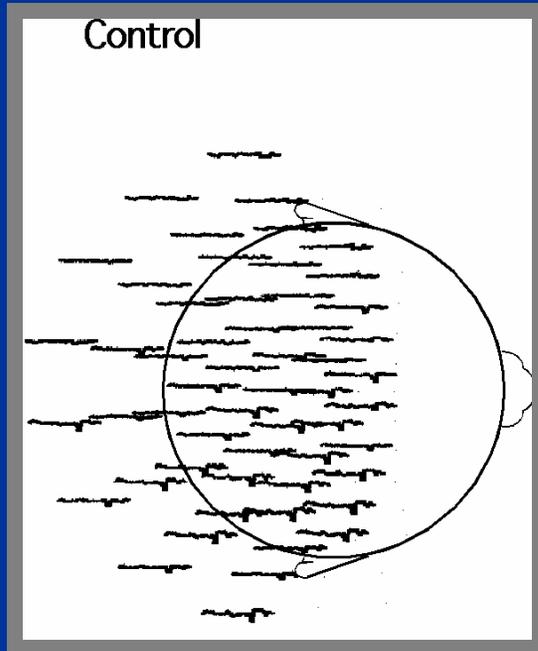
Stimulus for Migraine Studies

(8 Hz pattern reversal)



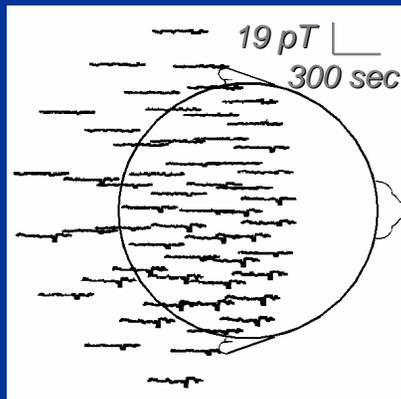
(Cao et al., Arch Neurol 56:548-554,1999)

DC-MEG Waveforms

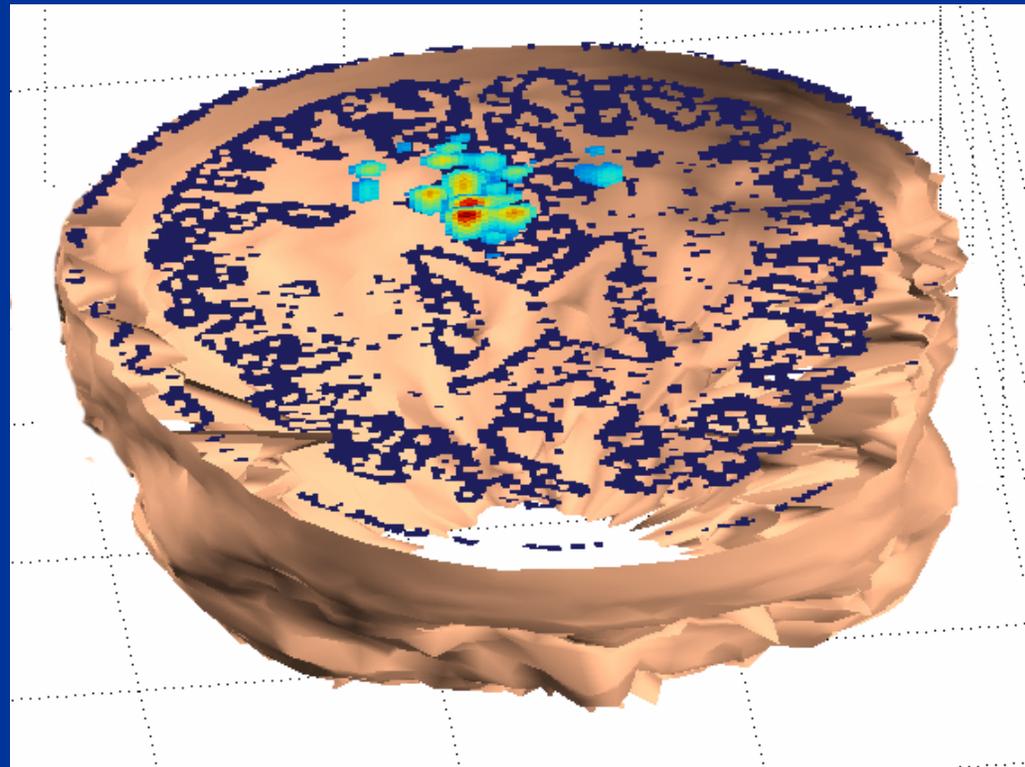
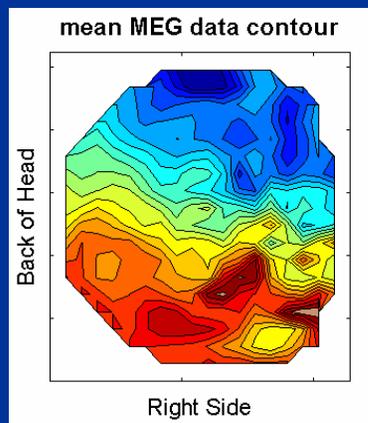


19 pTesla 
300 seconds

Control Subject

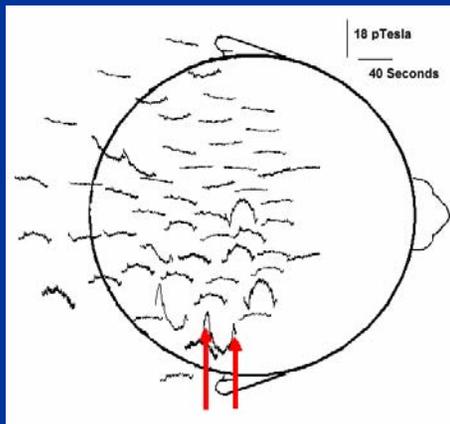


MEG data

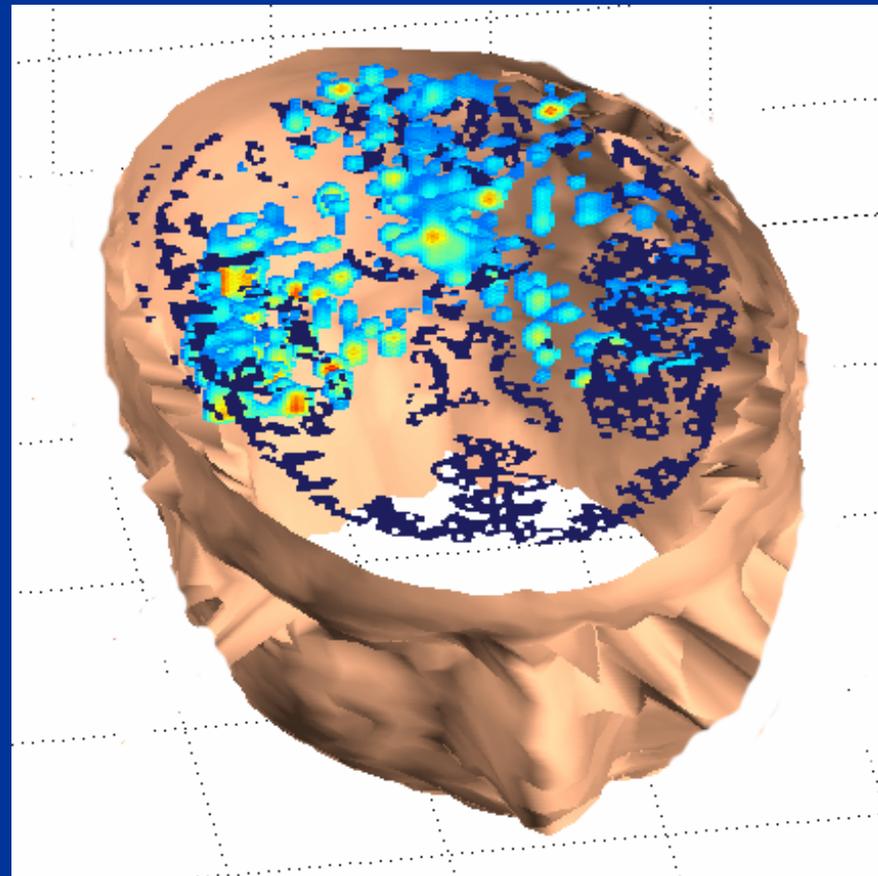
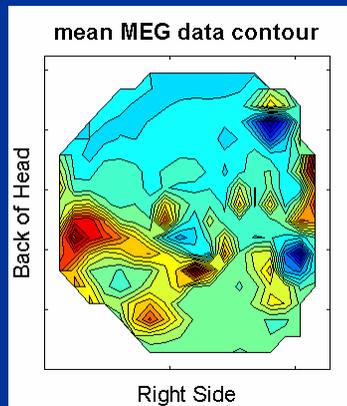


Mean cortical source
amplitudes

Evoked Migraine Subject

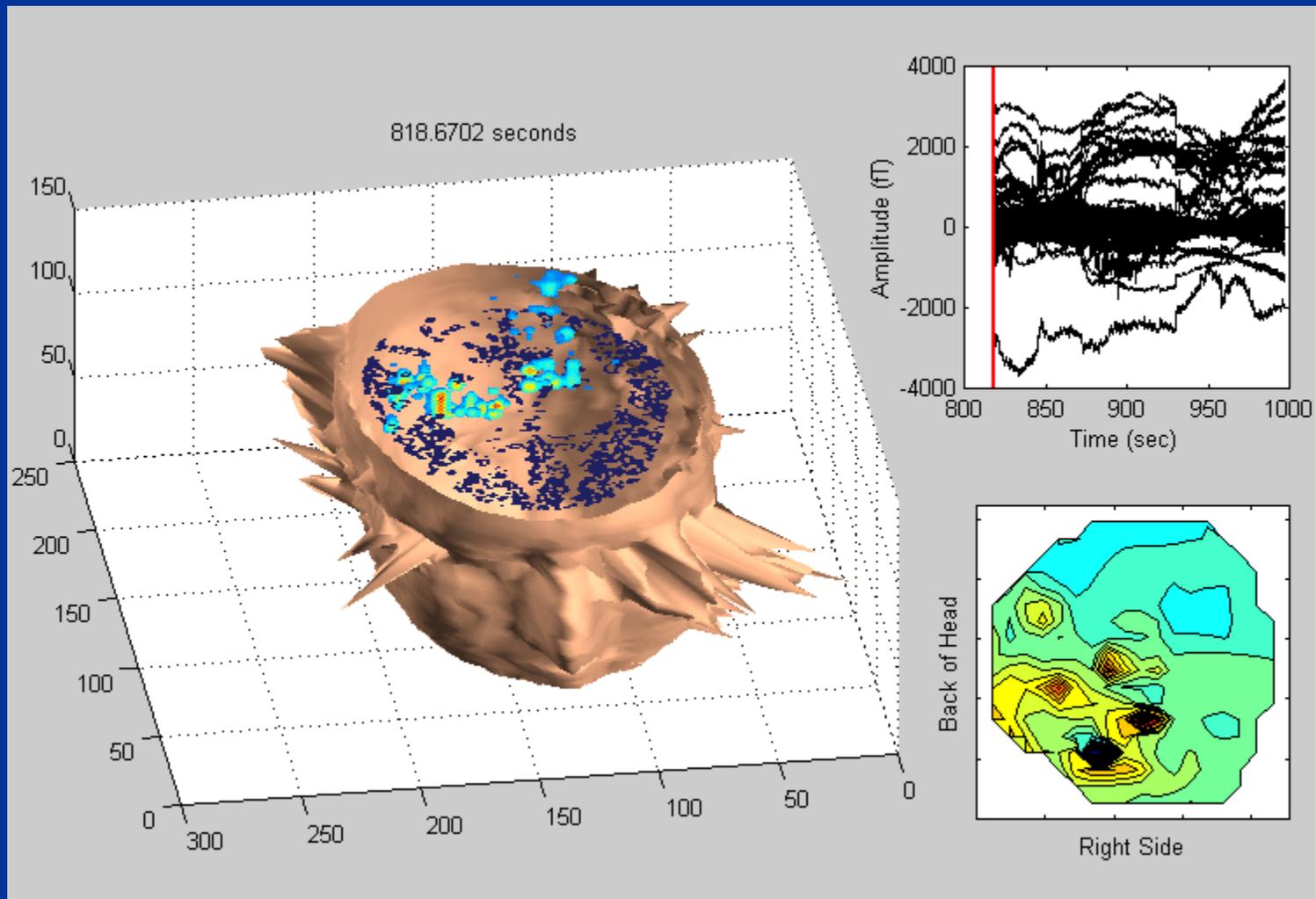


MEG data

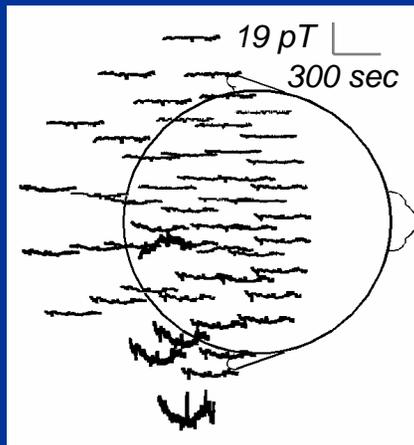


Mean cortical source amplitudes

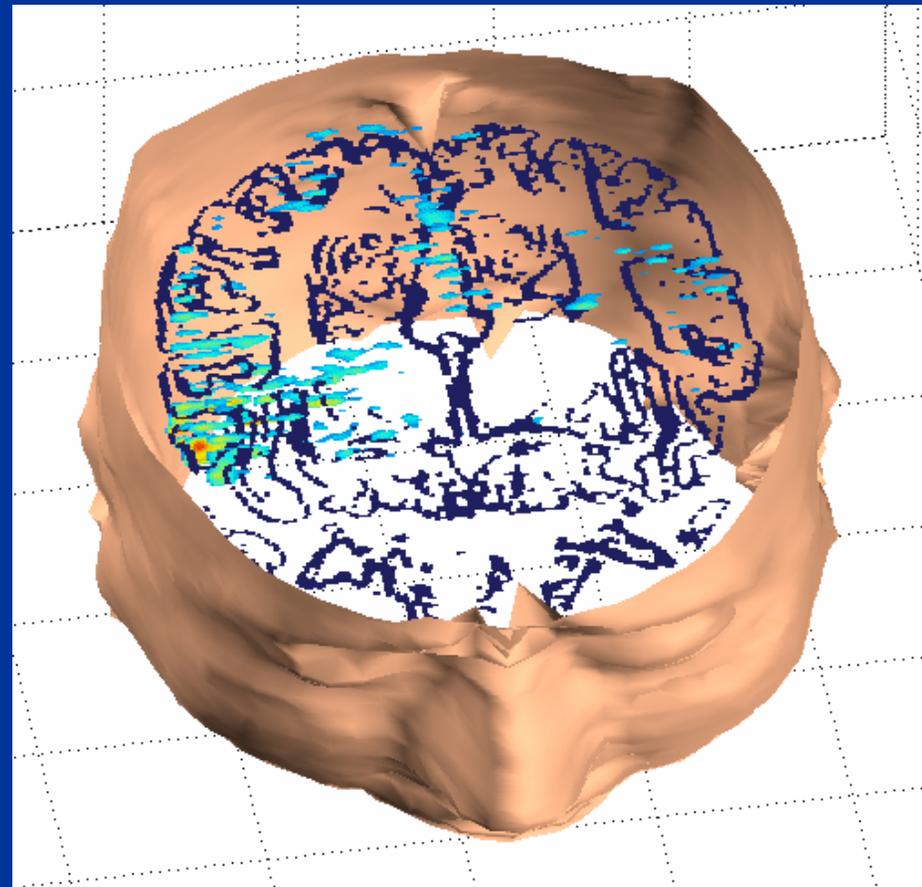
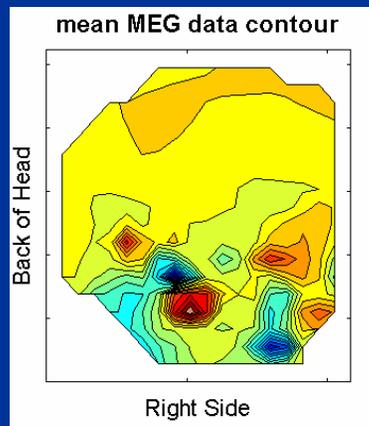
Evoked Migraine Subject



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 ± 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

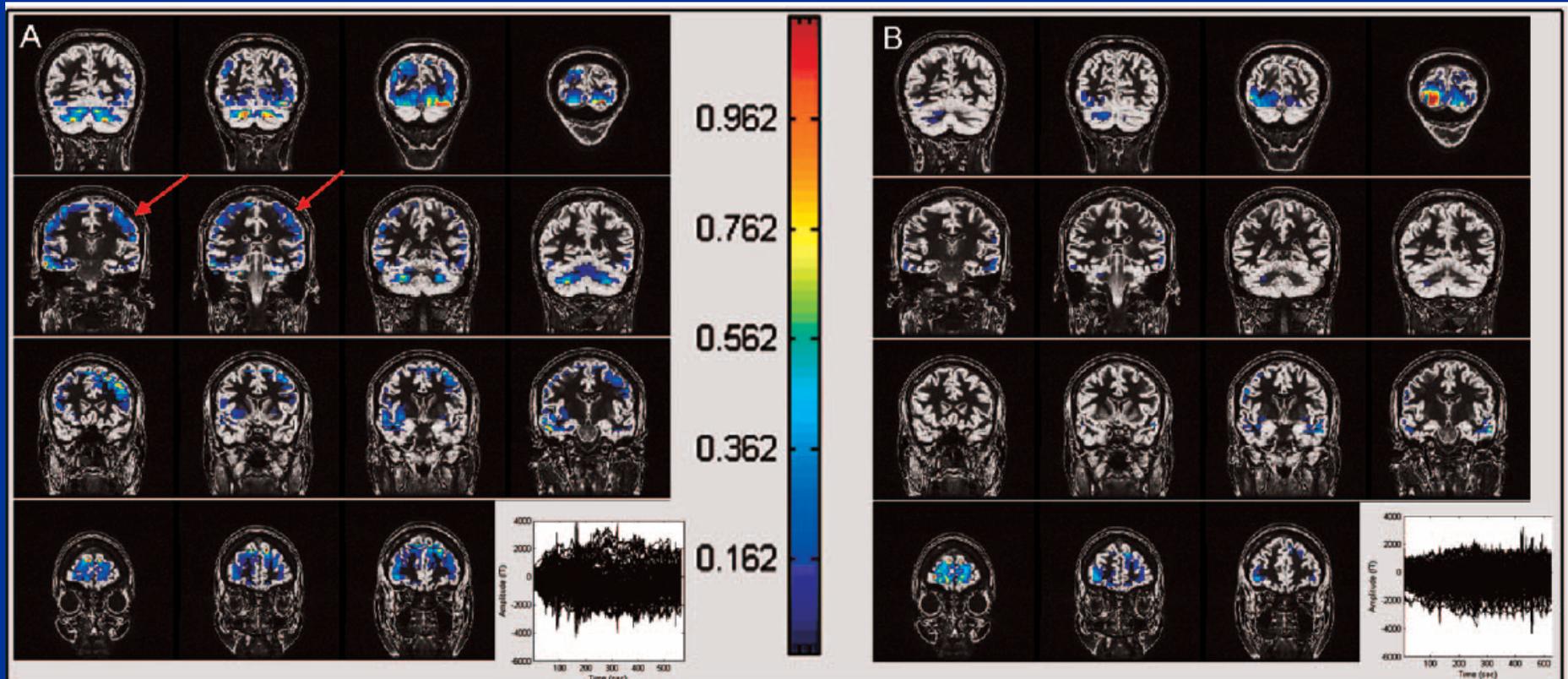
DC Shifts during spontaneous and induced migraine were larger in amplitude than controls.

DC-MEG Shifts reminiscent of SCD

Numerous studies support SCD as the underlying mechanism in Migraine.

These are difficult studies to perform as some patients moved, even though their heads were well secured.

Hyperexcited Occipital Cortex

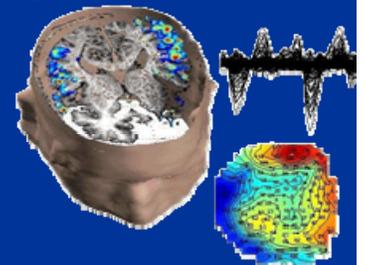


A) MR-FOCUSS analysis of the MEG recordings from a migraine patient before start of treatment with sodium valproate. Averaged MEG image activation results of cortical activity, over the initial 400 seconds. Scale is in nanoamp meters. Note the extended cortical areas of activation in the occipital, parietal (*large arrows*), and frontal cortex.

B) MR-FOCUSS analysis of the MEG recordings from the same migraine patient after 30 days of treatment. (Bowyer et al J Clin Neurophys 2005)

Advanced MEG Data Analysis for Looking at how Migraine Activity (SCD) can be Disrupted

- Independent component analysis (ICA)- source separation of multiple complex spatial signals
- Current density- allows extended patterns of currents to be mapped
MR-FOCUSS - Multi Resolution FOCal Underdetermined System Solver
- Coherence- a measure of synchronization between brain regions. Synchronized activity within a neuronal network is determined by the strength of network connections. Focal regions that sporadically drive the network will exhibit high coherence with all other regions.



Coherence Imaging: Calculation

1. Calculate time sequence of brain activity
 - a. ICA extraction of burst activity brain source signals
 - b. MR-FOCUSS (current density) imaging of ICA components
2. Calculate FFT sequence
3. Calculate cross-spectral density between sources by multiplying the Fourier-transformed signals (frequency space) of the time series.
4. Calculate coherence matrix by normalizing the cross spectral density with the power spectral density of both time series. Its values ranges from 0 (no similarity) to 1 (identical time series).
5. Calculate average coherence, each source for 1-30Hz.

Extracting real-time neural networks from MEG data

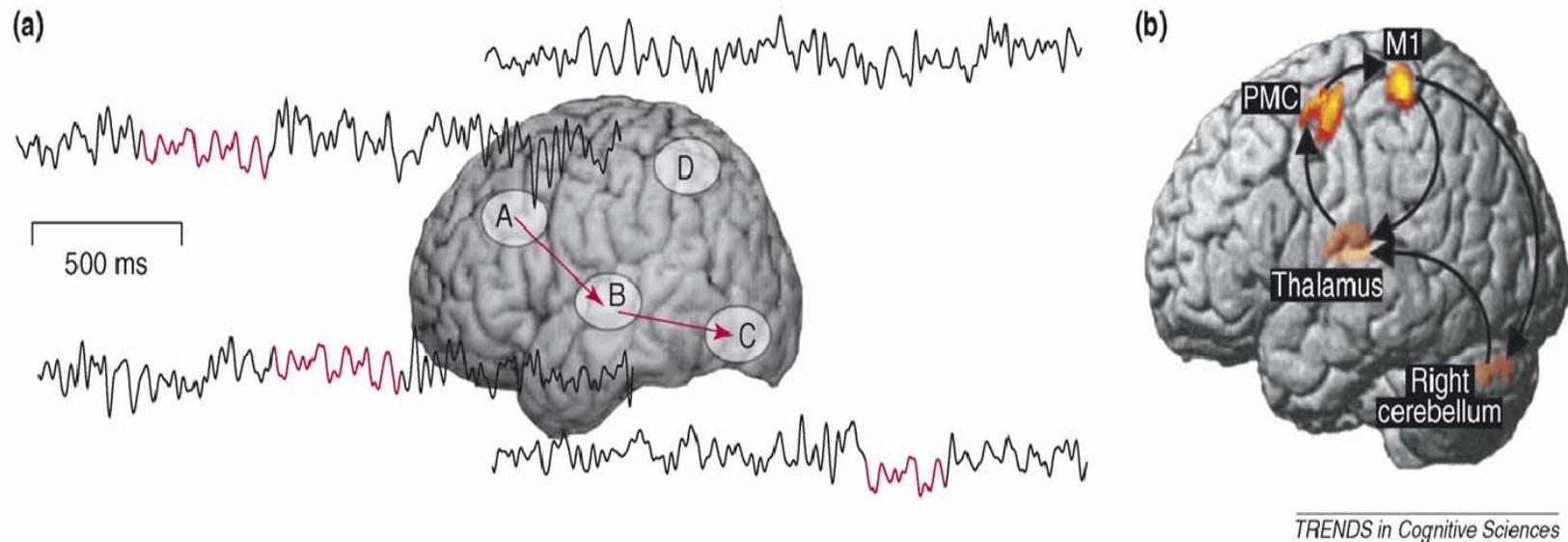
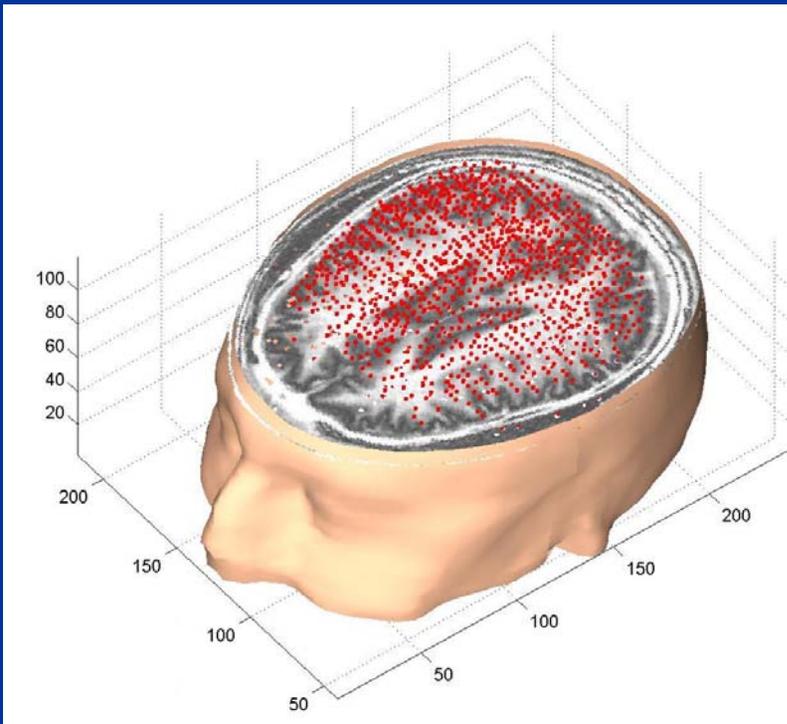


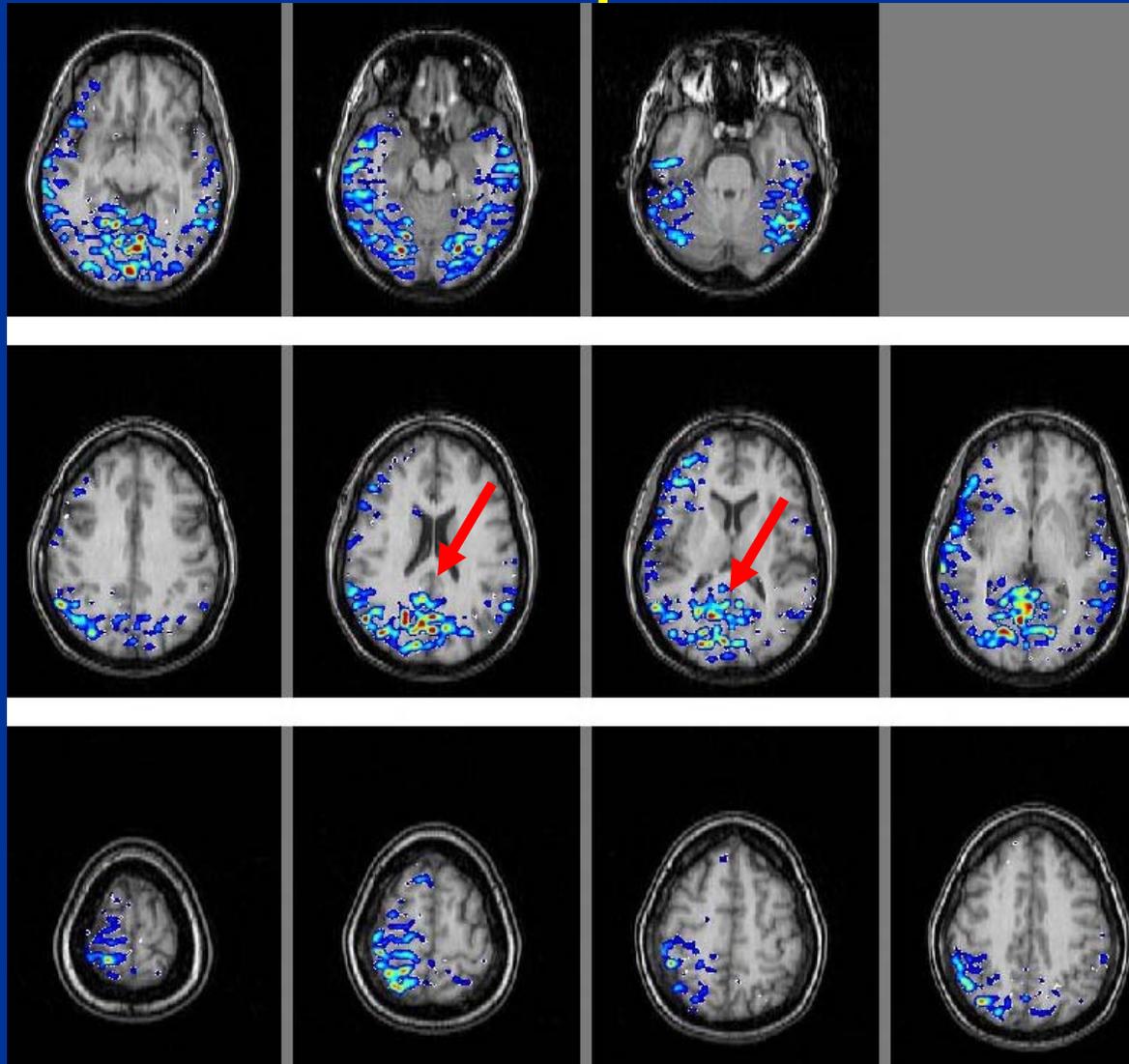
Figure 1. Extracting long-range neural connectivity from MEG data. **(a)** Simplified presentation of the basic idea. Curves depict time courses of activity in four brain areas (gray ellipses). If neuronal populations in these areas are functionally connected, one would expect to detect similar time courses of activation in the different areas (red segments), at least occasionally. Time shifts between similar stretches of activity could be interpreted as flow of information. In this example, one could argue that there is a drive from area A to B and a weaker drive further to area C. Delays between the repeated segments are exaggerated. **(b)** Neural network during slow movements of the right index finger. Here, EMG from the moving finger provided a meaningful, nonbrain reference signal. EMG–MEG coherence led to the contralateral motor cortex, which served as a reference area for identification of the network within the brain. Abbreviations: M1, primary motor cortex; PMC, premotor cortex. Reproduced, with permission, from Ref. [48].

Cortical Model

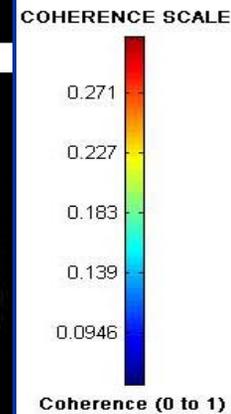


- Created from Volumetric MRI Data
- 4,000 cortical locations
- 3 dipoles at each location that represent x, y, z
- Distribution matches cortical gray matter

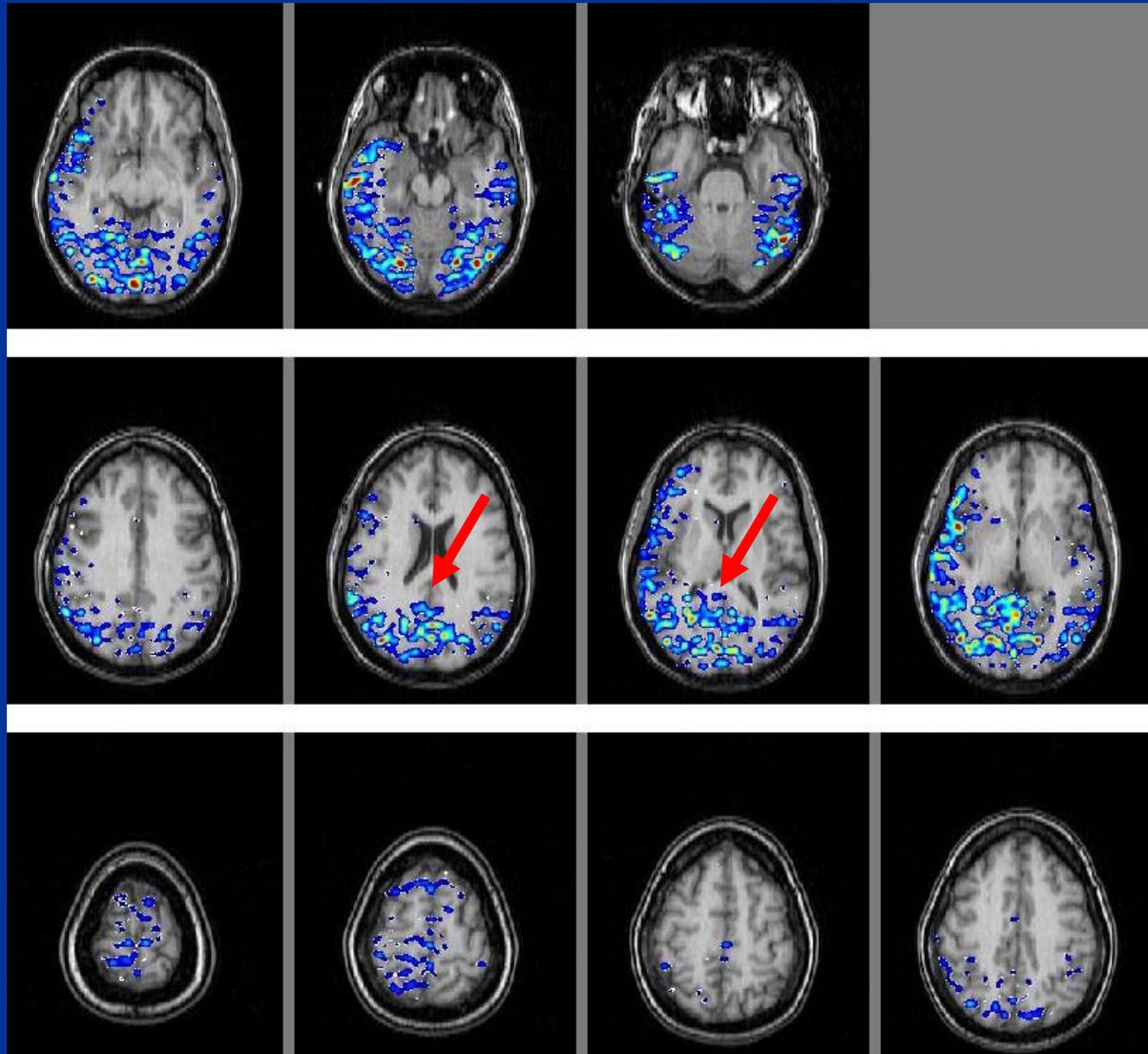
Coherence in Migraine Patient pre treatment



Regions of high coherence prior to treatment 18 minutes of 8 Hz visual stimulation



Coherence in Migraine Patient 20 minutes post treatment



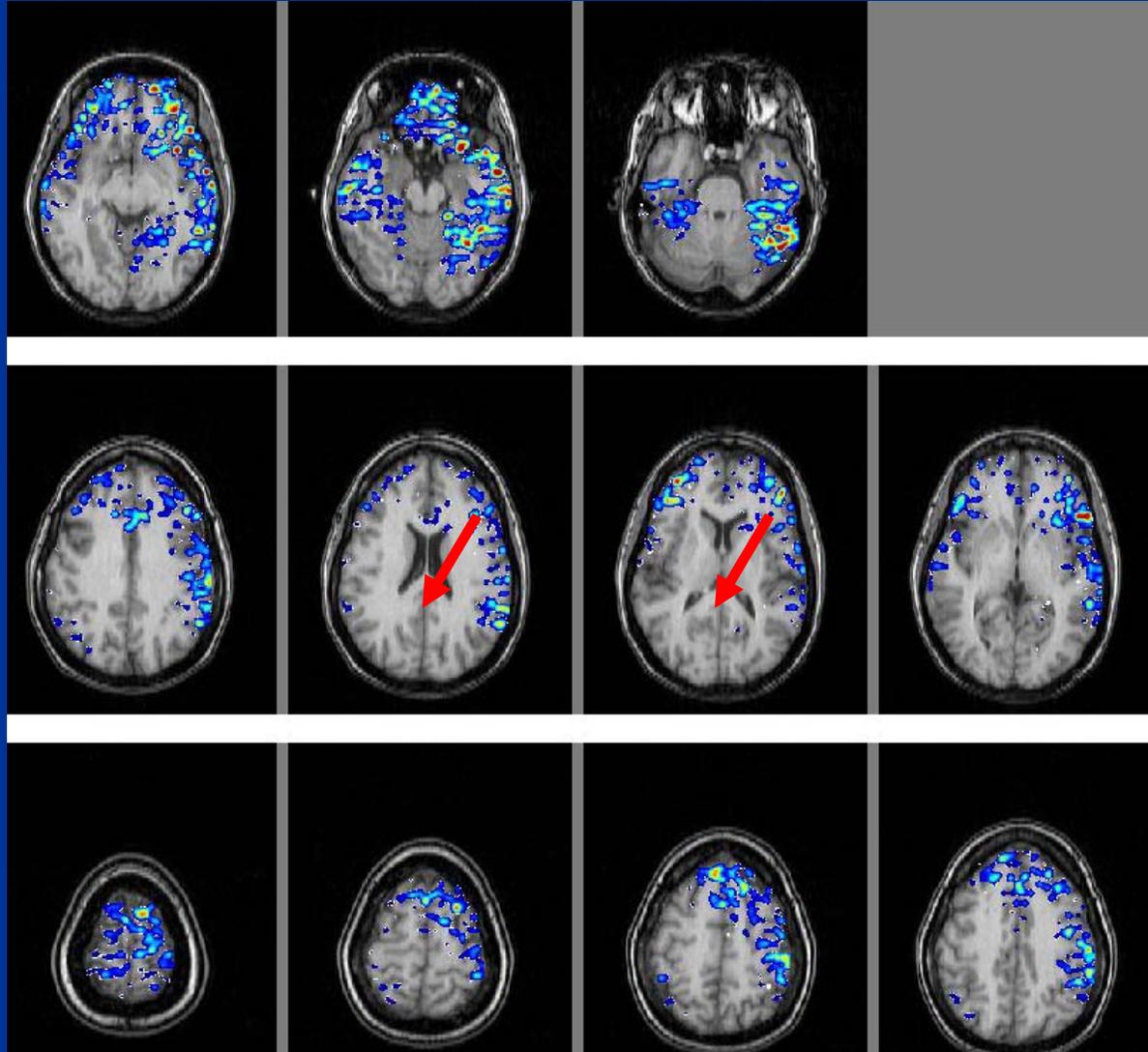
Coherence in the occipital cortex has been reduced after treatment

COHERENCE SCALE



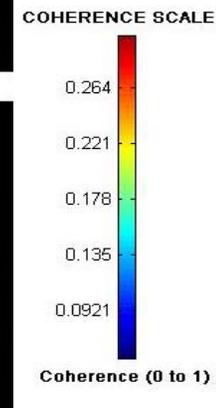
Coherence (0 to 1)

Coherence in Migraine Patient 30 DAYS post treatment



Coherence in the occipital cortex has been disrupted after treatment.

This patient has had no Migraine in the past 28 days.



Coherence Analysis Results for Migraine Treatment

11 Patients with migraine	Coherence Reduced	Coherence Not reduced
Headache reduced	6	1
Headaches Not reduced	2	2

- 2 Control subjects had small reduction in coherence in the occipital cortex compared to migraine patients over 30days.

Conclusion

- Further analysis on specific frequency bands may provide more information on the migraine patient's cortical networks.
- Other headache types (chronic, cluster) should be included for comparison.
- This method would be easier to implement
- This may also lead to a more complete understanding of the neurological disturbances linked to SCD.

Thank you for your attention.

MEG_TOOLS

**a complete MEG analysis software
package** (requires Matlab)

available at www.megimaging.com

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