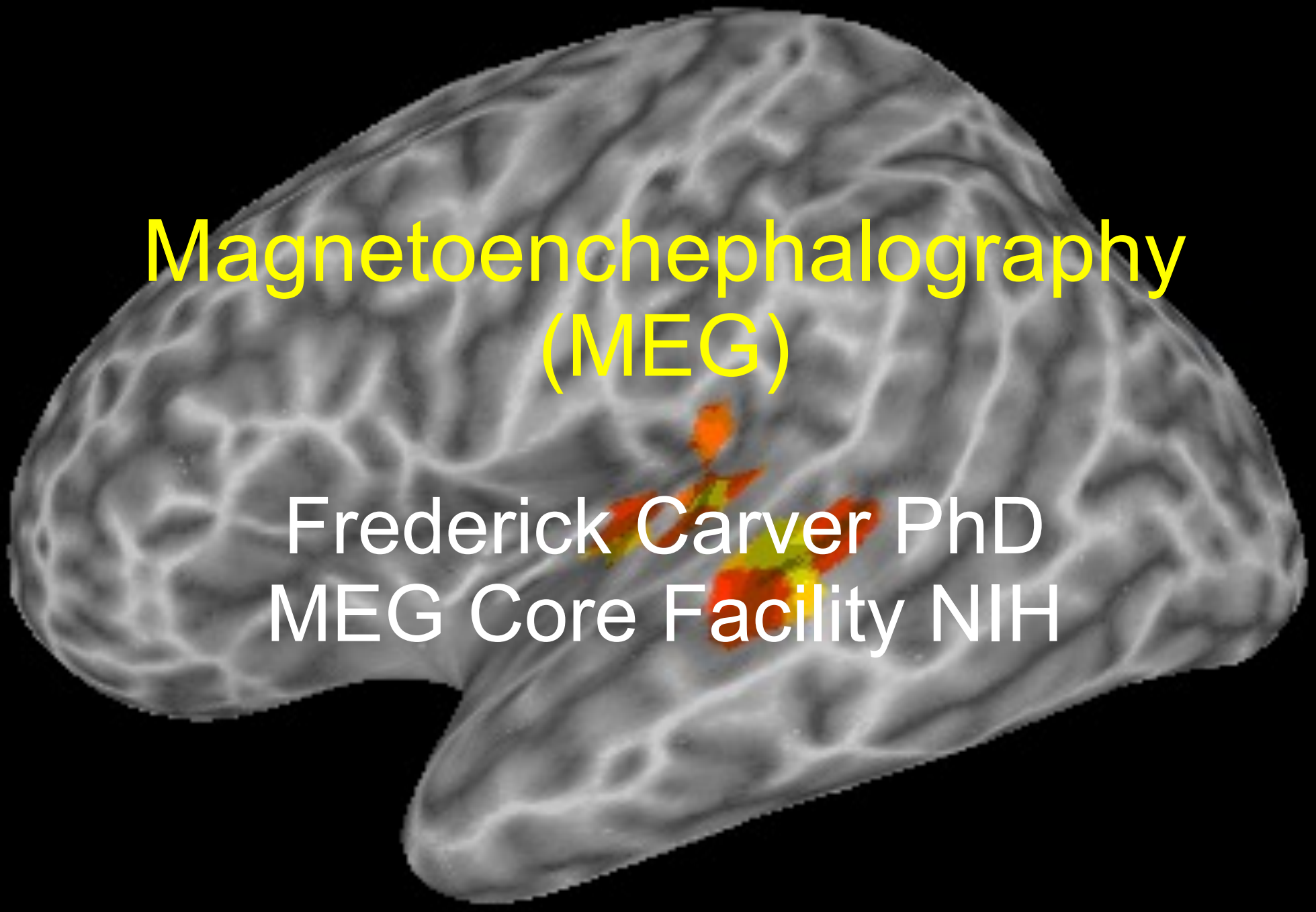
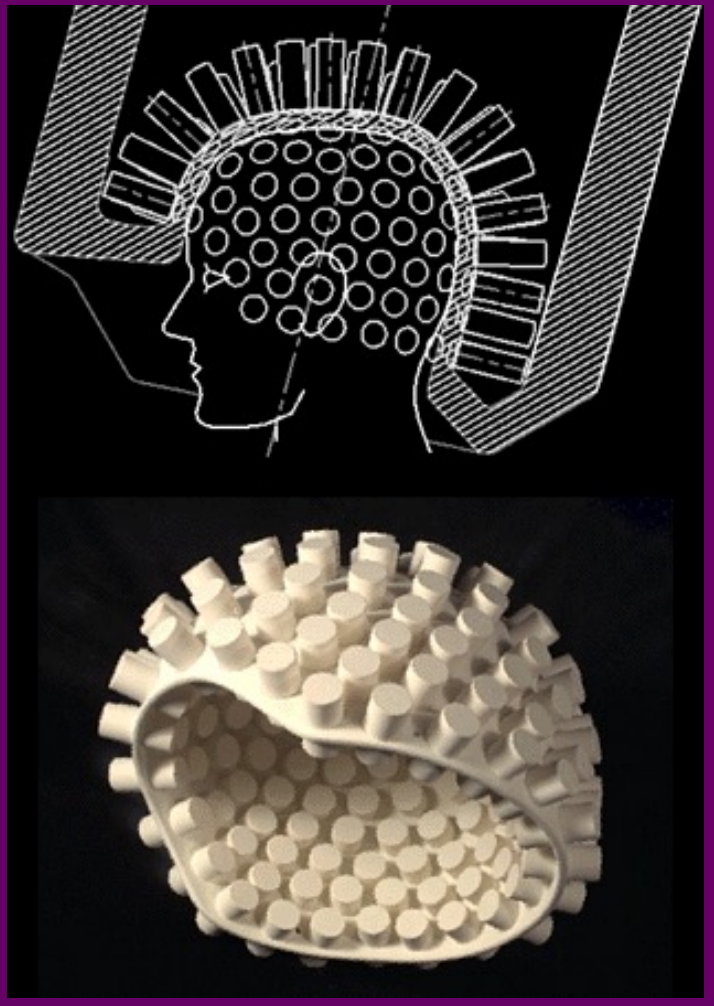


Magnetoenchephalography (MEG)

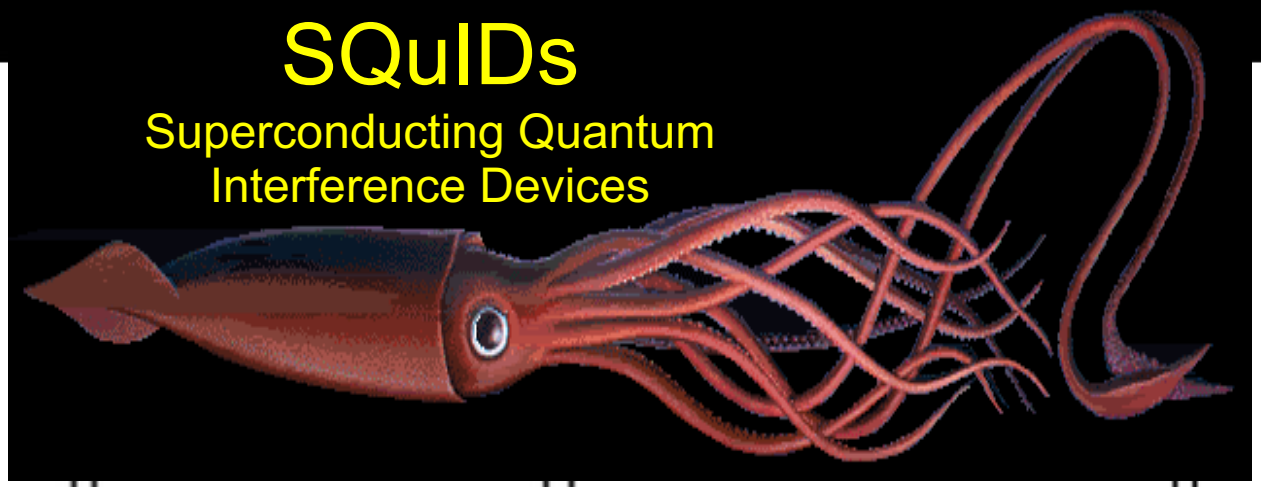
Frederick Carver PhD
MEG Core Facility NIH

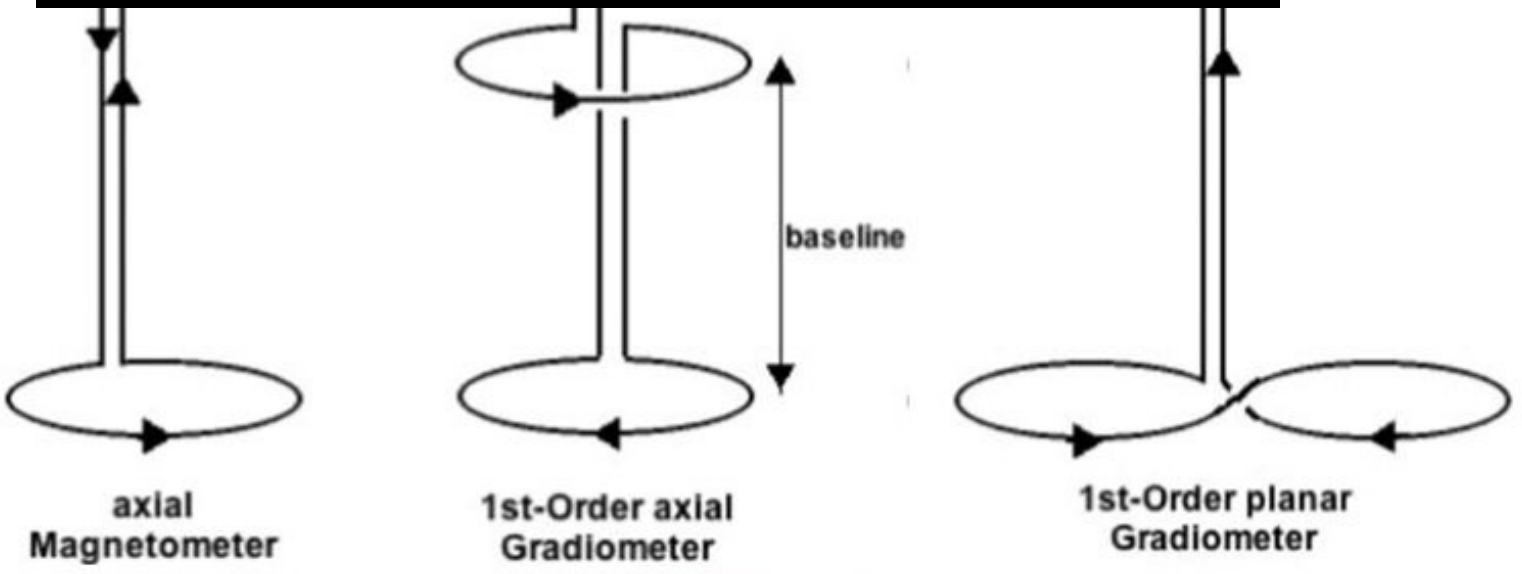
Our CTF system has 275 radial gradiometers, and 30 reference sensors (also EEG).



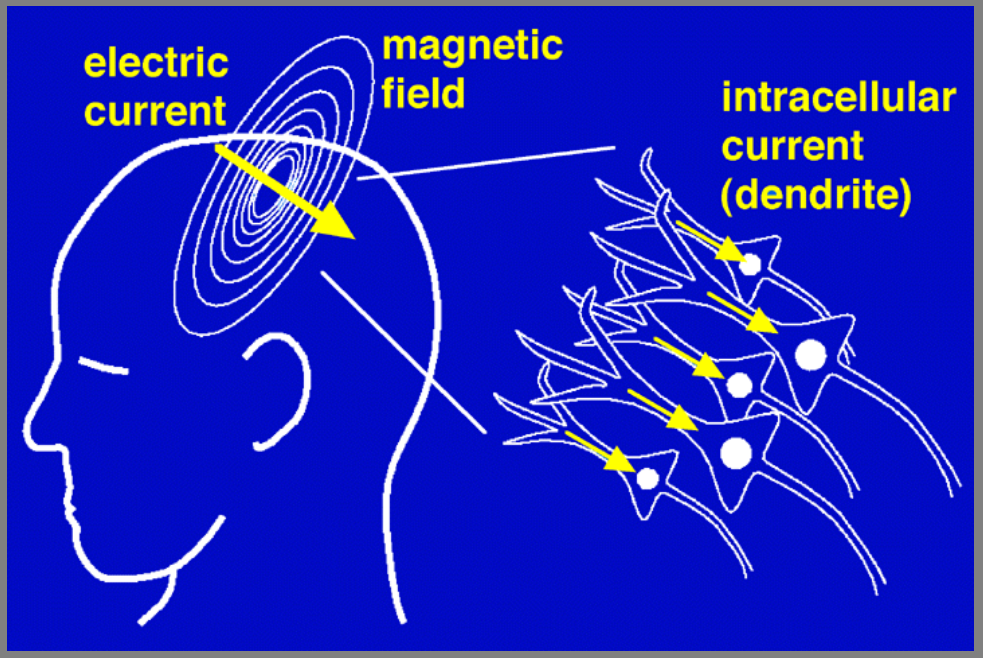
SQuIDs

Superconducting Quantum Interference Devices





Signal Source



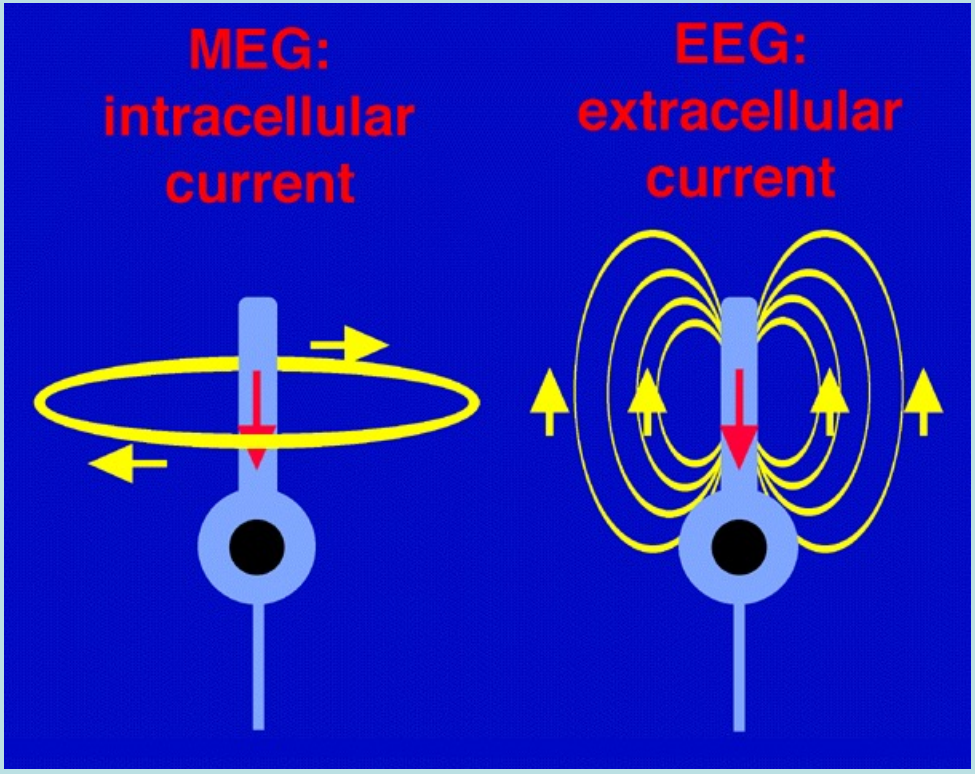
The long apical dendrites of cortical pyramidal cells are the theoretical source of MEG signals

Up to 10,000 parallel cells need to be active to produce measurable fields outside the head

A typical evoked field is on the order of 100 femto Tesla

($1fT = 10^{-15}T$)

Comparison to EEG

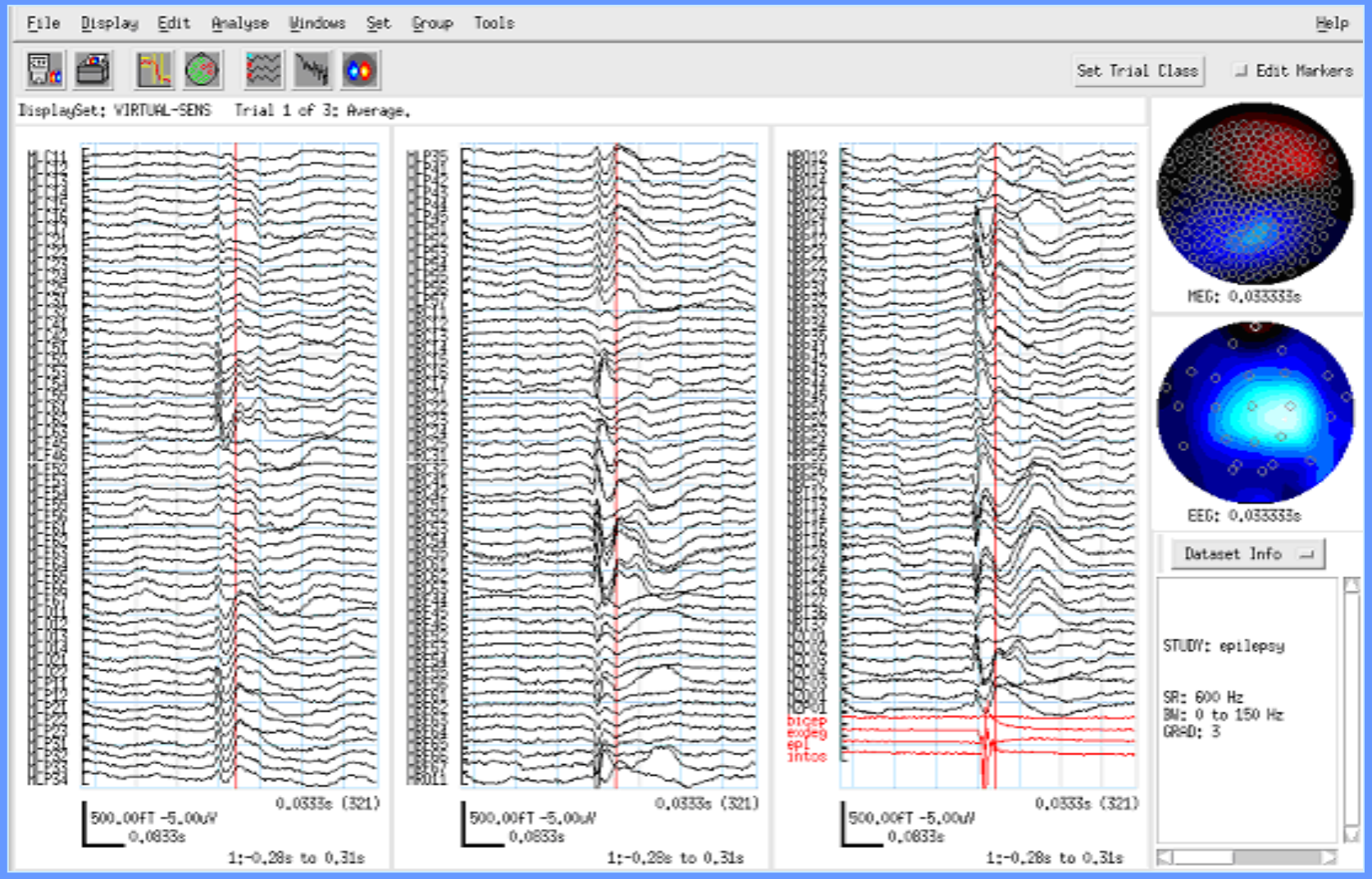


Magnetic fields pass through the skull without interference

Volume conduction distorts EEG signals making source reconstruction difficult

Some sources may be harder to see with MEG because of orientation, or cancellation. e.g. SMA

MEG Example



Epileptic spike associated with muscle twitch

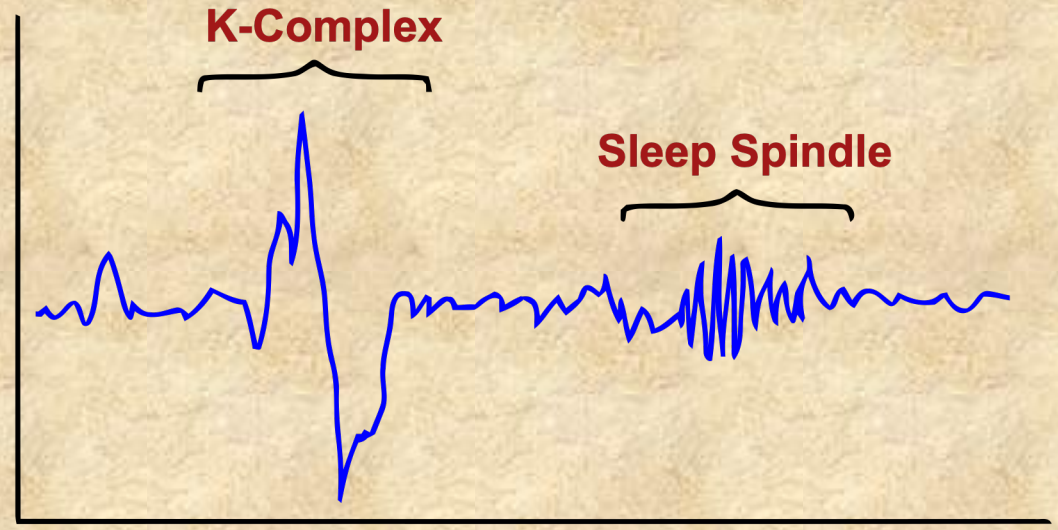
Sato et al.,
NINDS

Time Series Analysis

What are we looking for?

- Individual spikes or complex waveforms
  e.g. epileptic spike, sensory evoked response

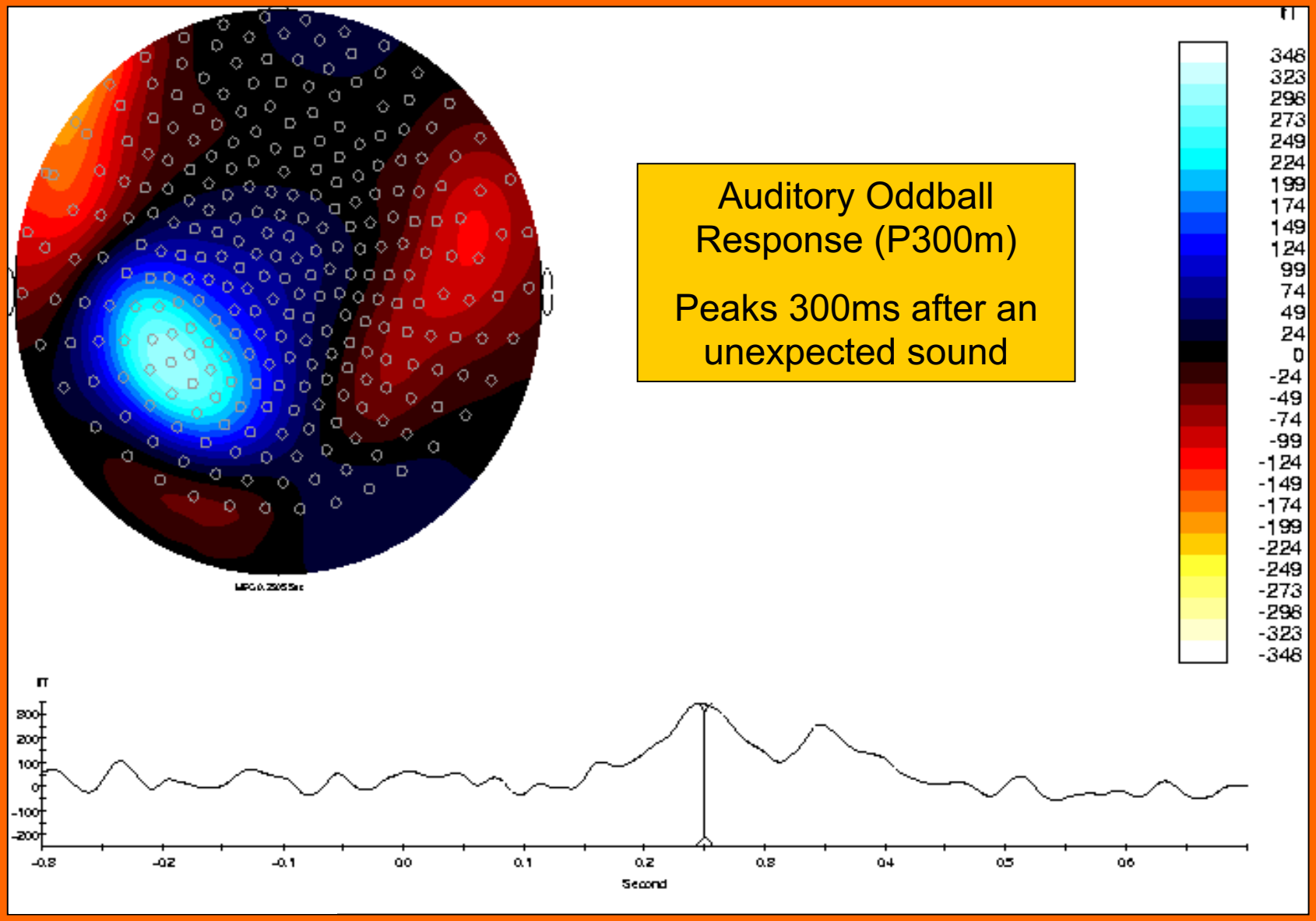
- Oscillations at particular frequency bands
  e.g. theta (4-8Hz), alpha (8-13Hz), beta (14-30Hz), gamma (30-50Hz)



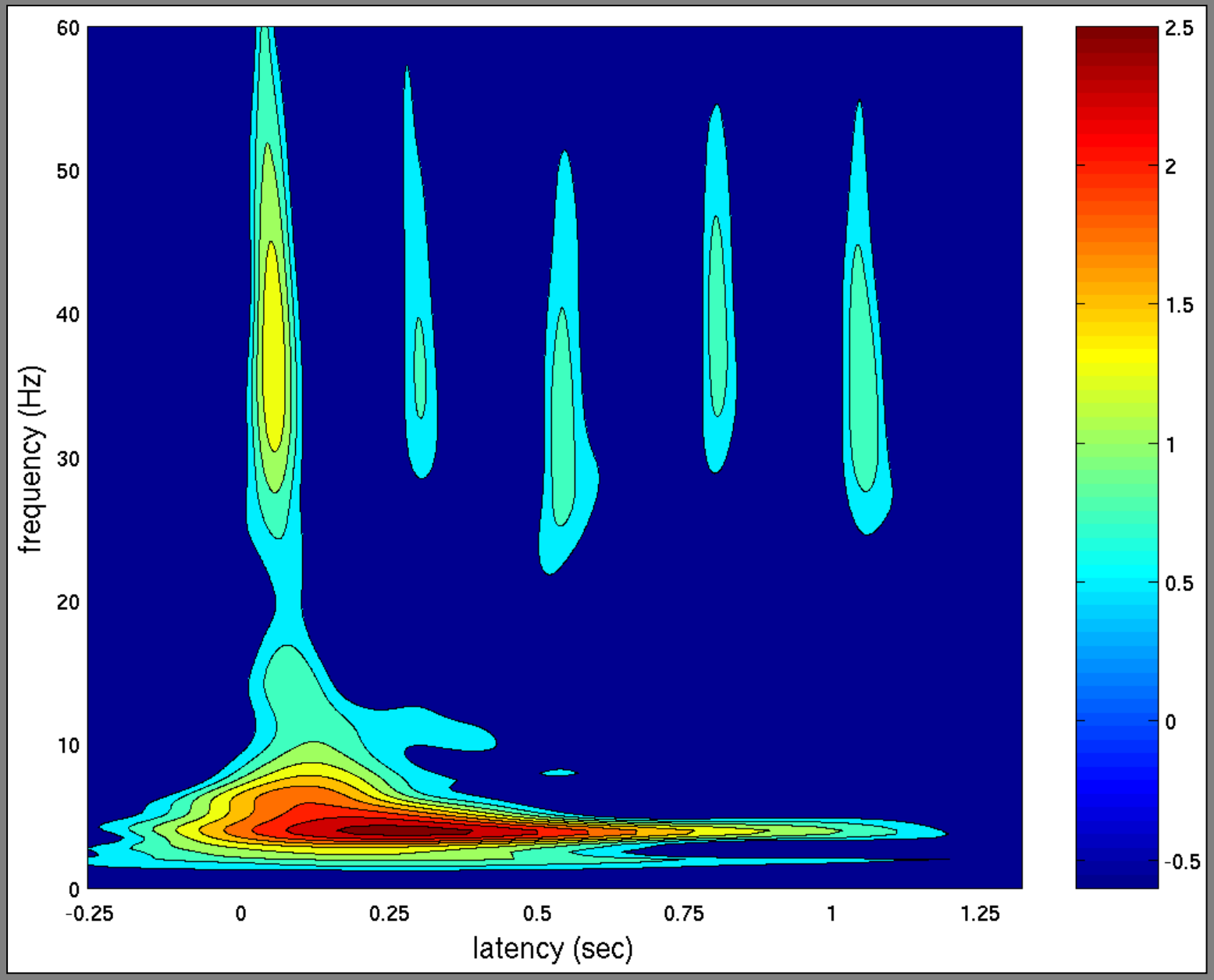
-wikipedia

Signal Averaging (Evoked/Event-related Fields)

- Average MEG time segments from similar stimuli/responses
- Quantify amplitude and/or peak latency of resulting ERFs

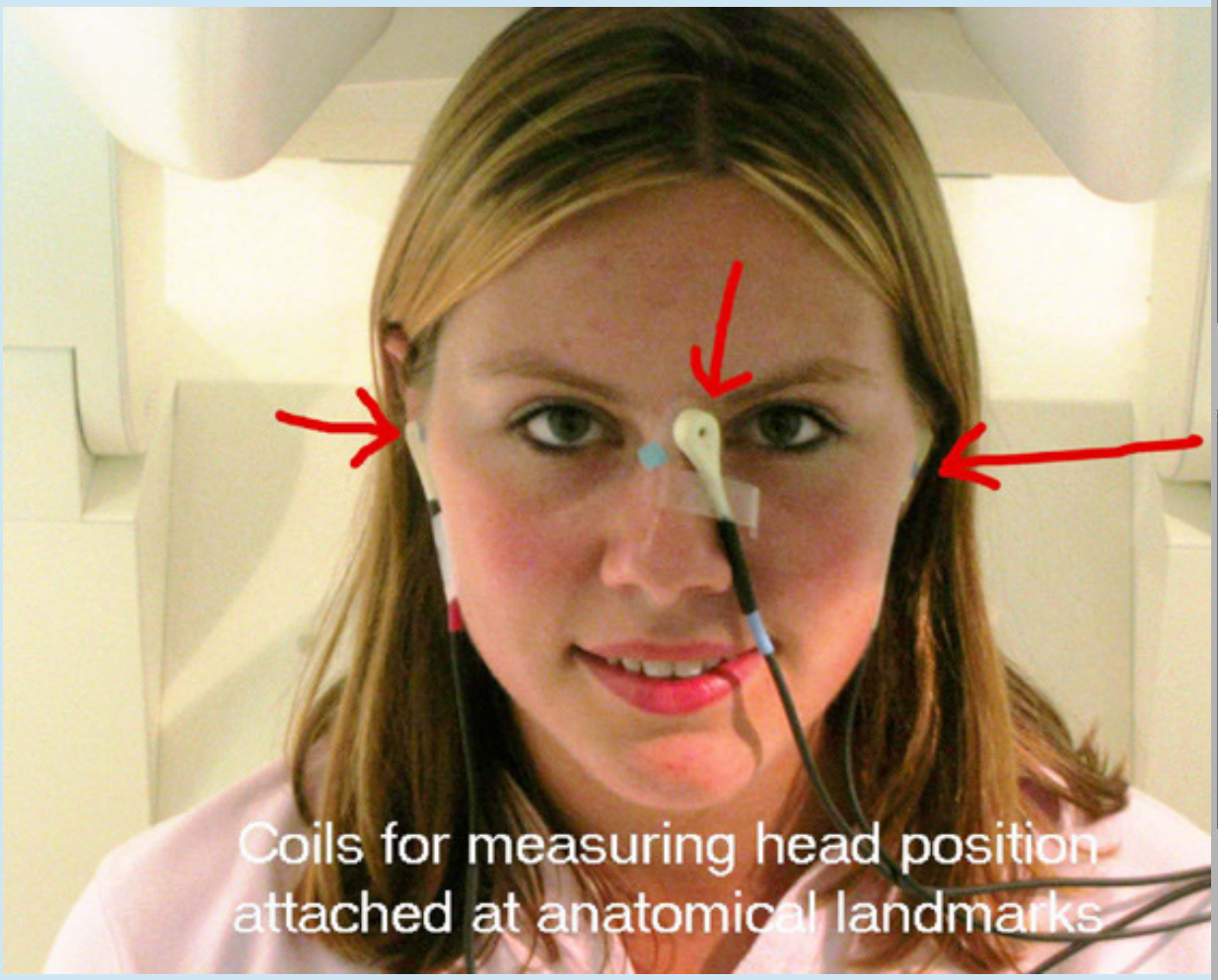


Time-frequency Analysis

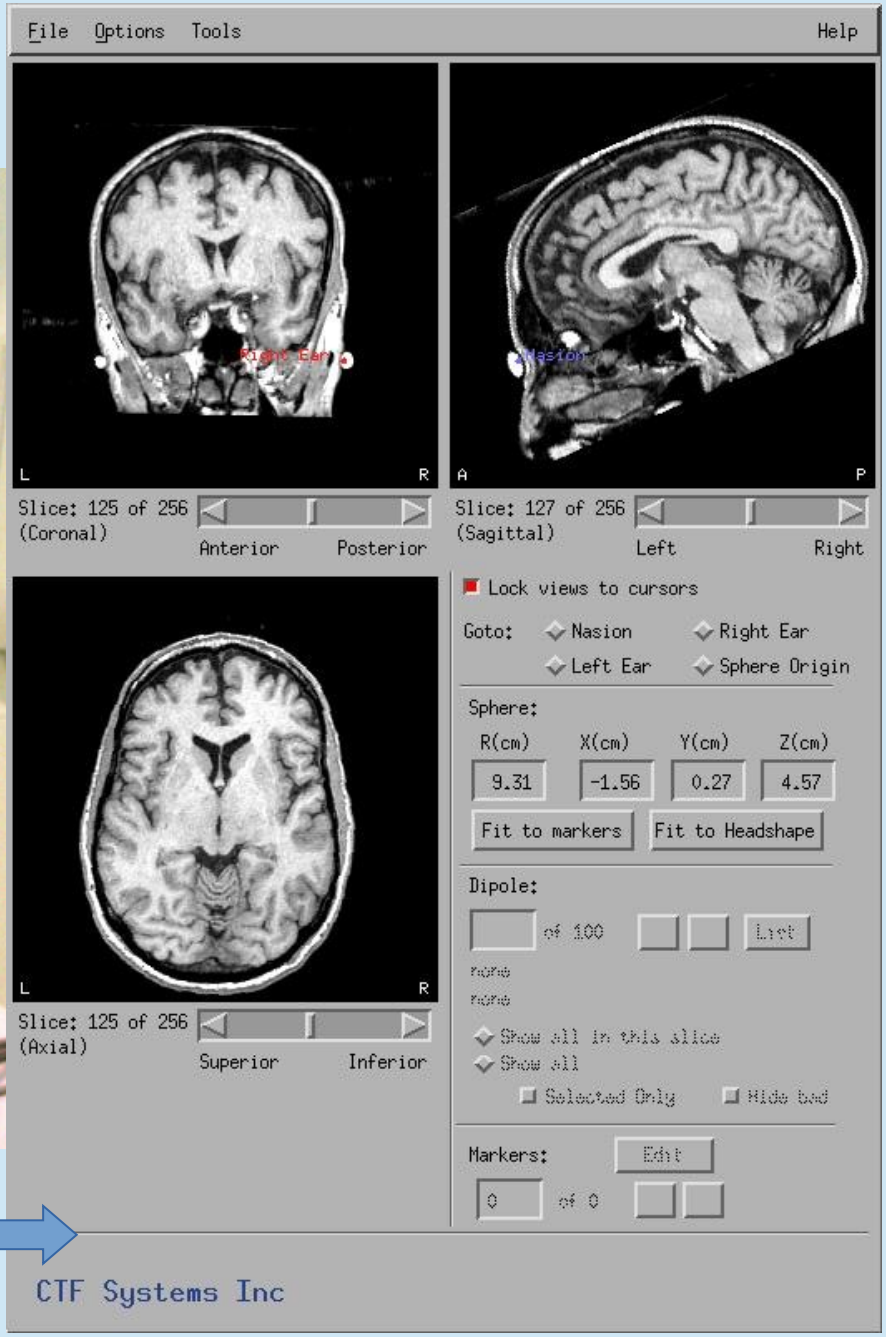


Evoked Response to series of five clicks separated by 250ms

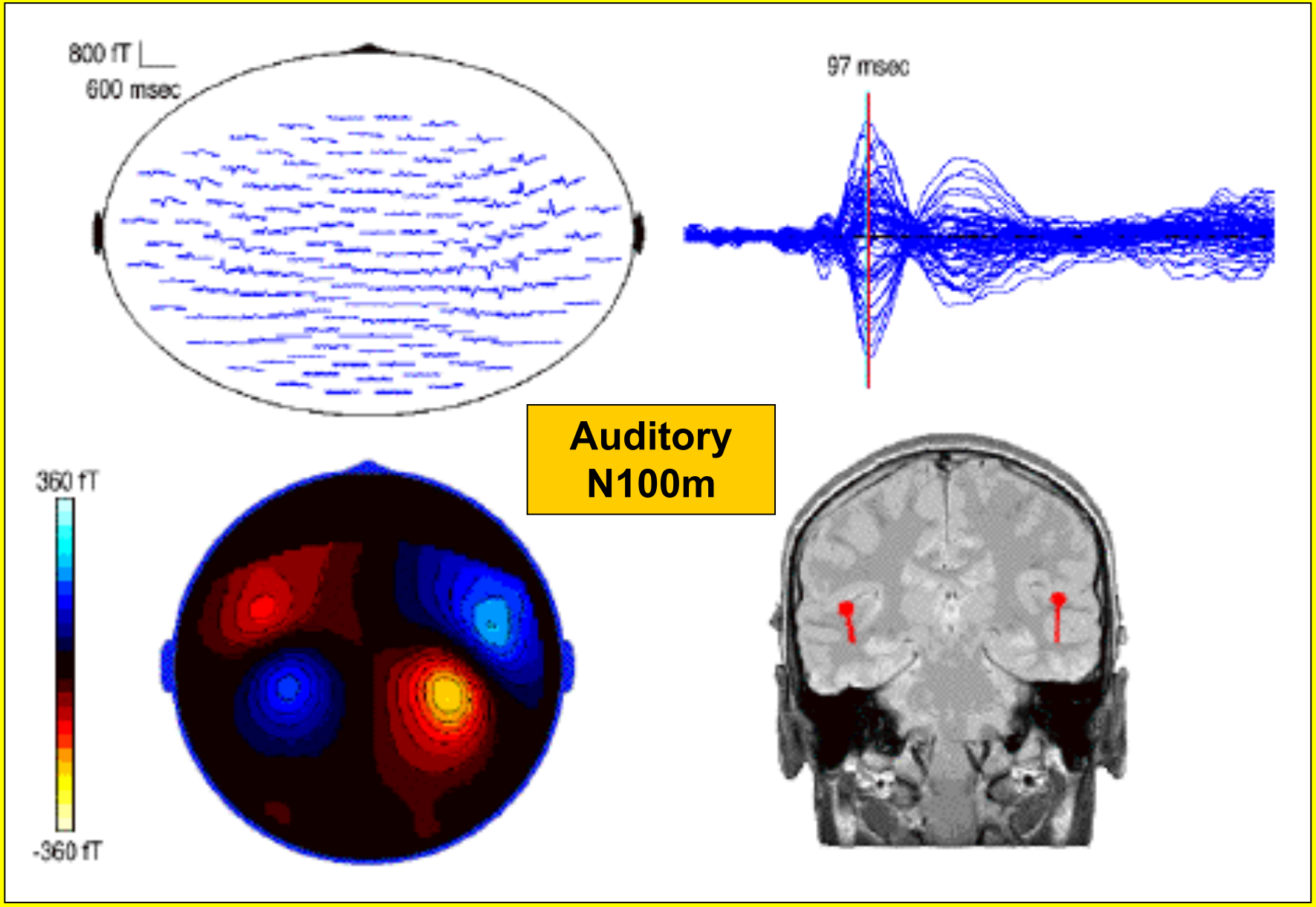
How do we estimate the source of the MEG signals?



The coil locations are then marked on an MRI for co-registration



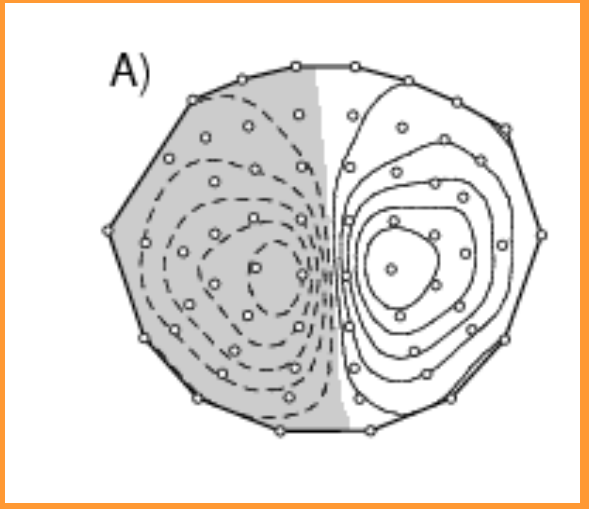
Dipole Fit



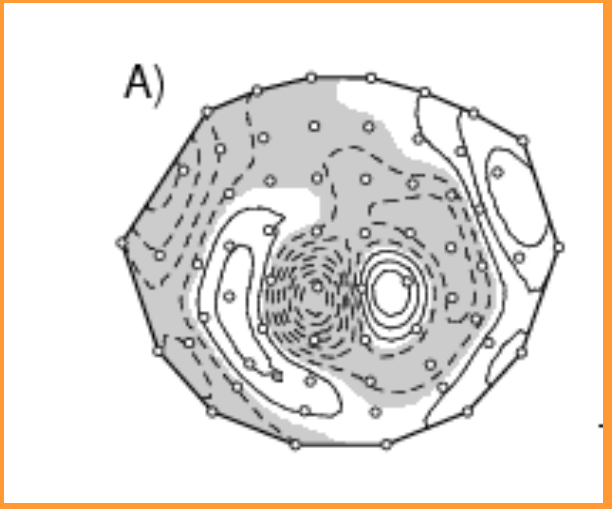
Find the one or more sources that best fit data at single time point

SAM (Synthetic Aperture Magnetometry)

- Produces whole brain estimates of source power for specified time window and frequency band
- Creates a spatial filter (beamformer) for each voxel to block out activity from other locations
  - Not good for correlated sources
  - Can generate ‘virtual channels’ at each voxel
- Subject group analysis can be conducted with AFNI or other fMRI software

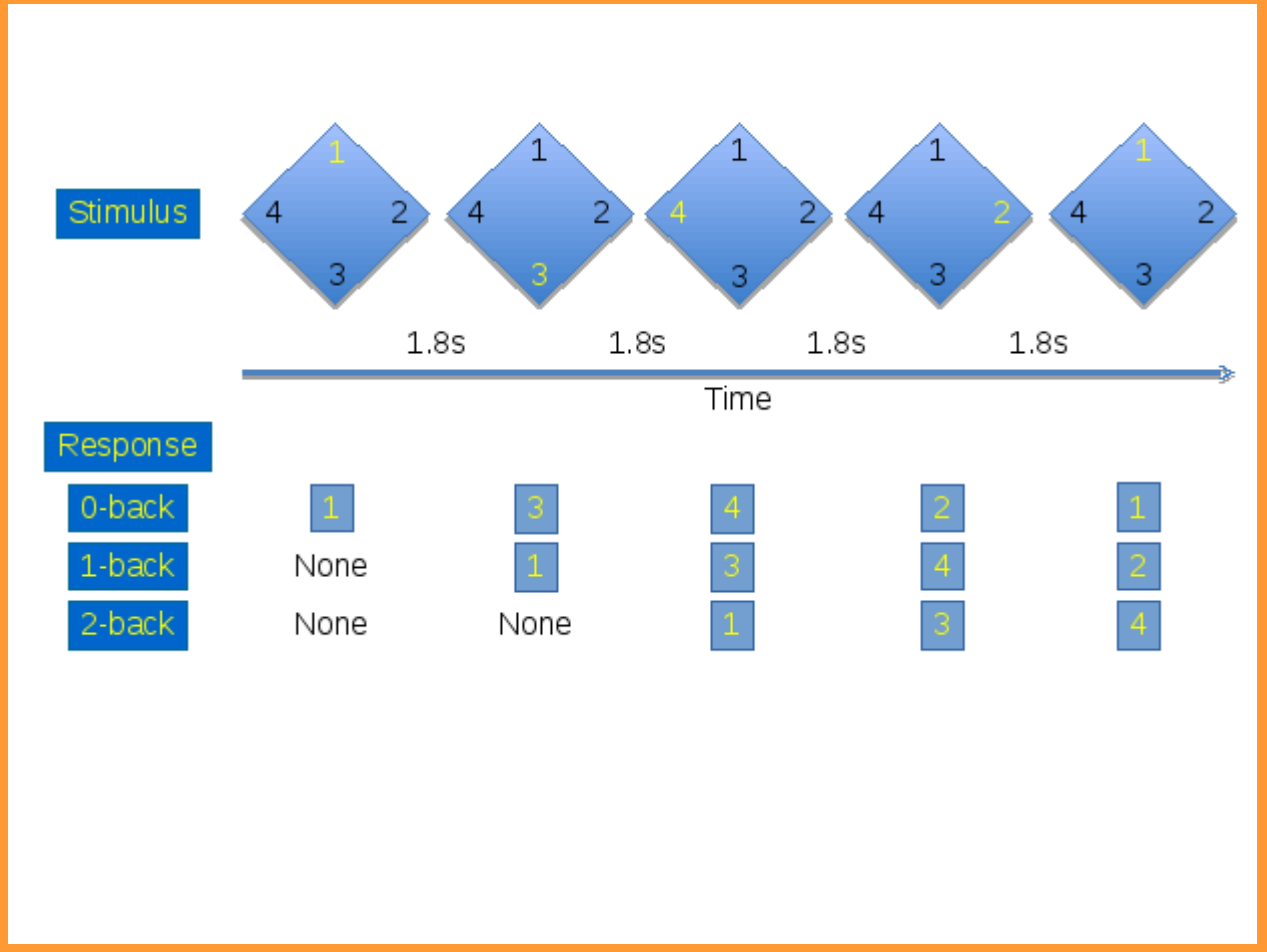


Projection or Source onto Sensors

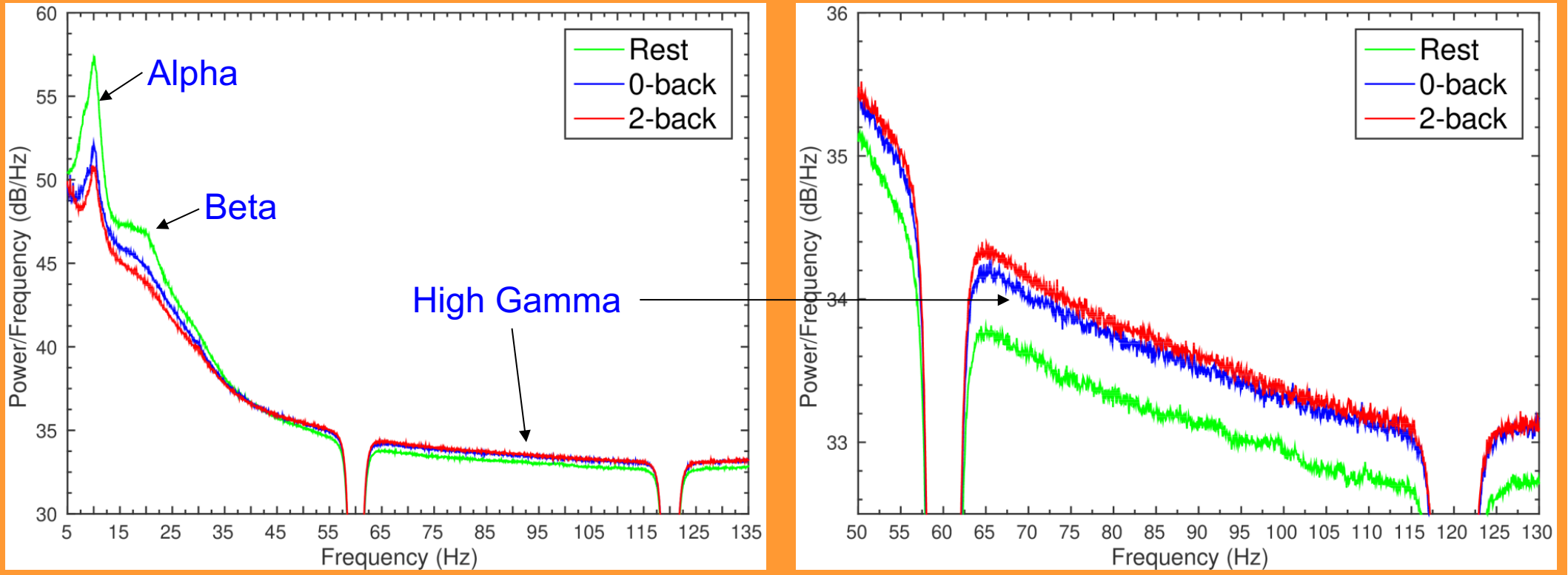


Spatial Filter

Example of SAM Analysis for an N-back working memory task with resting data used as a baseline



Power Spectra used to determine frequency bands for SAM Analysis



Carver et al., submitted

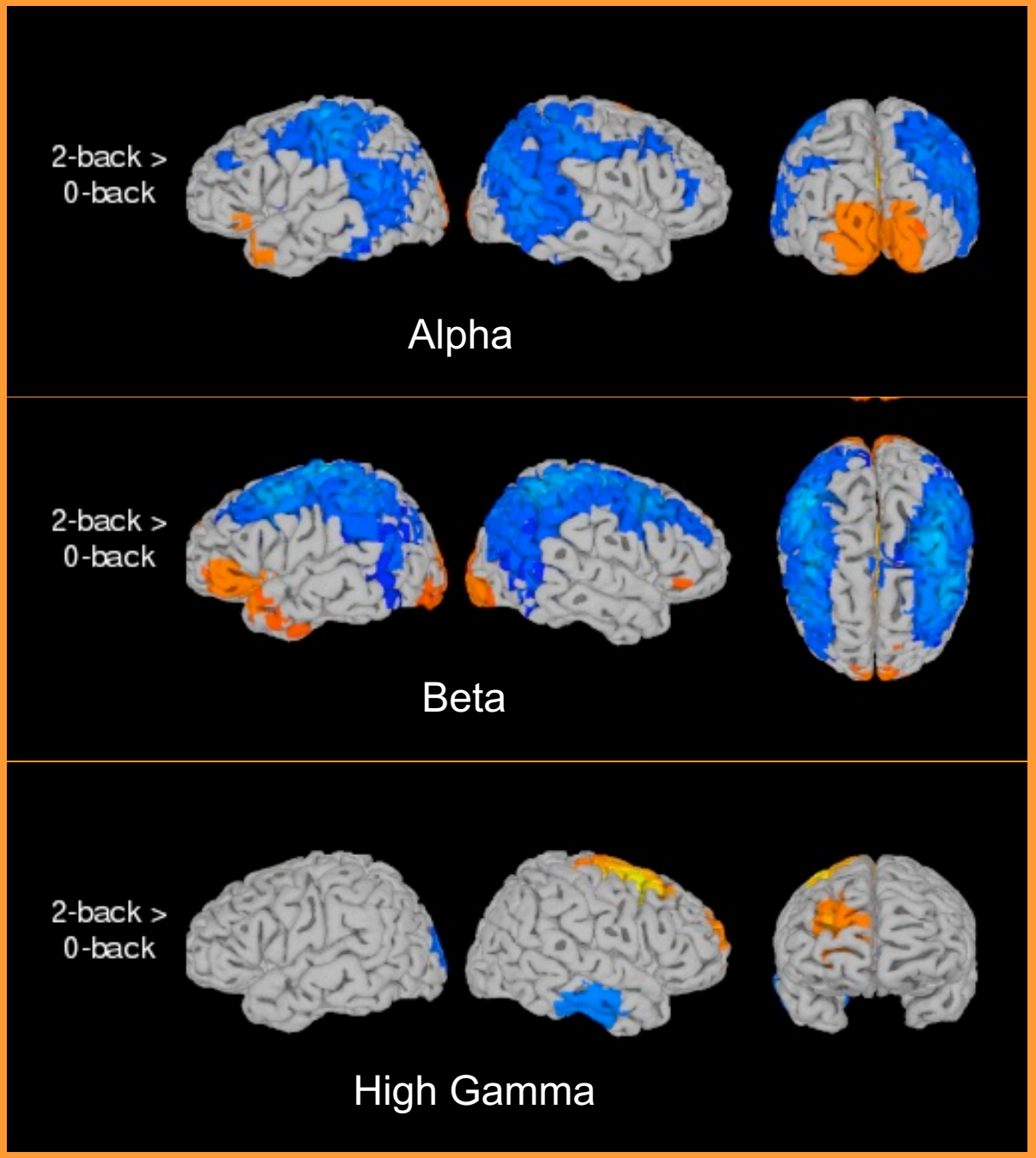
Red = 2 > 0

‘synchronization’ ?

Blue = 2 < 0

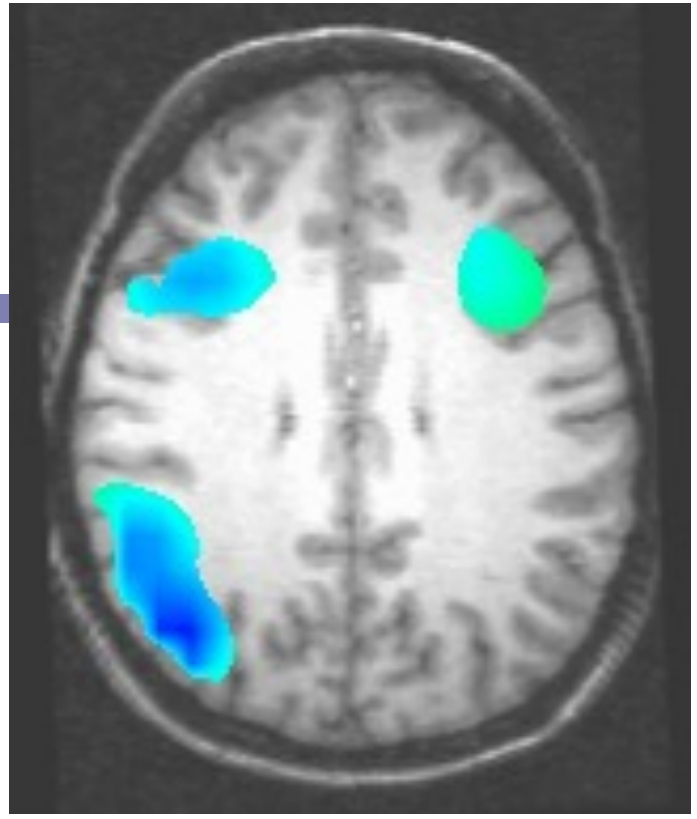
‘desynchronization’ ?

High Gamma = Spiking?

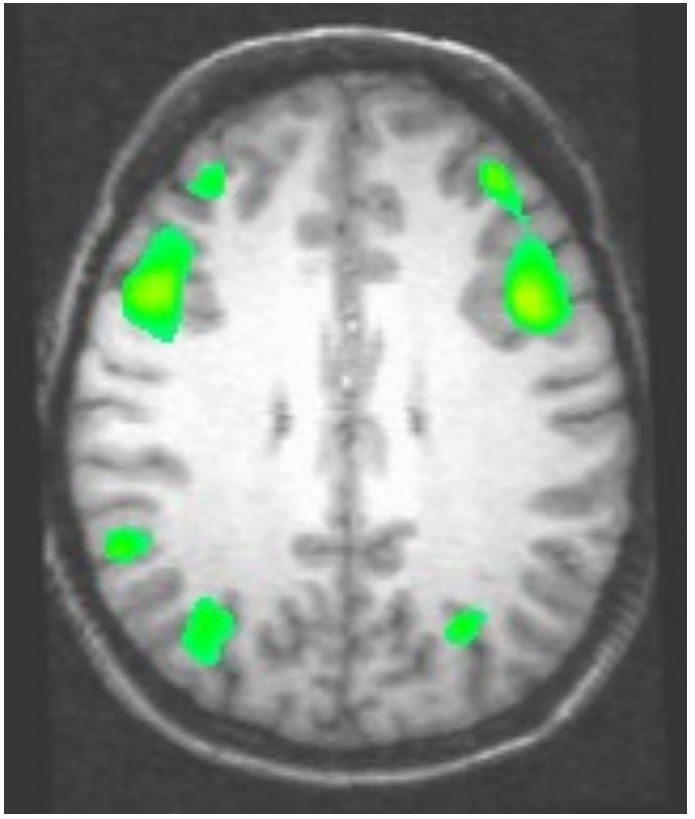


MEG and fMRI

2-back vs 0-back, same 12 subjects

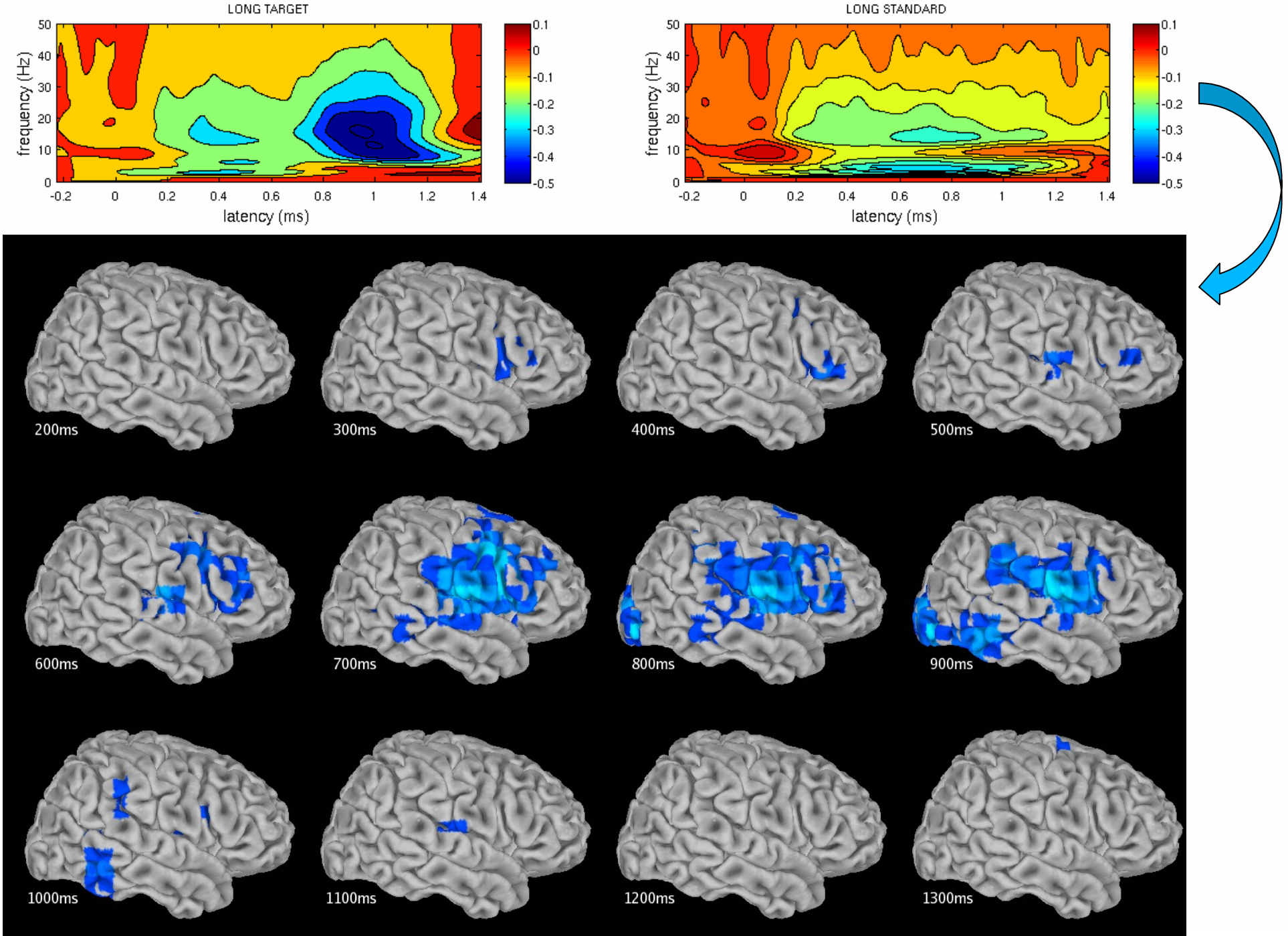


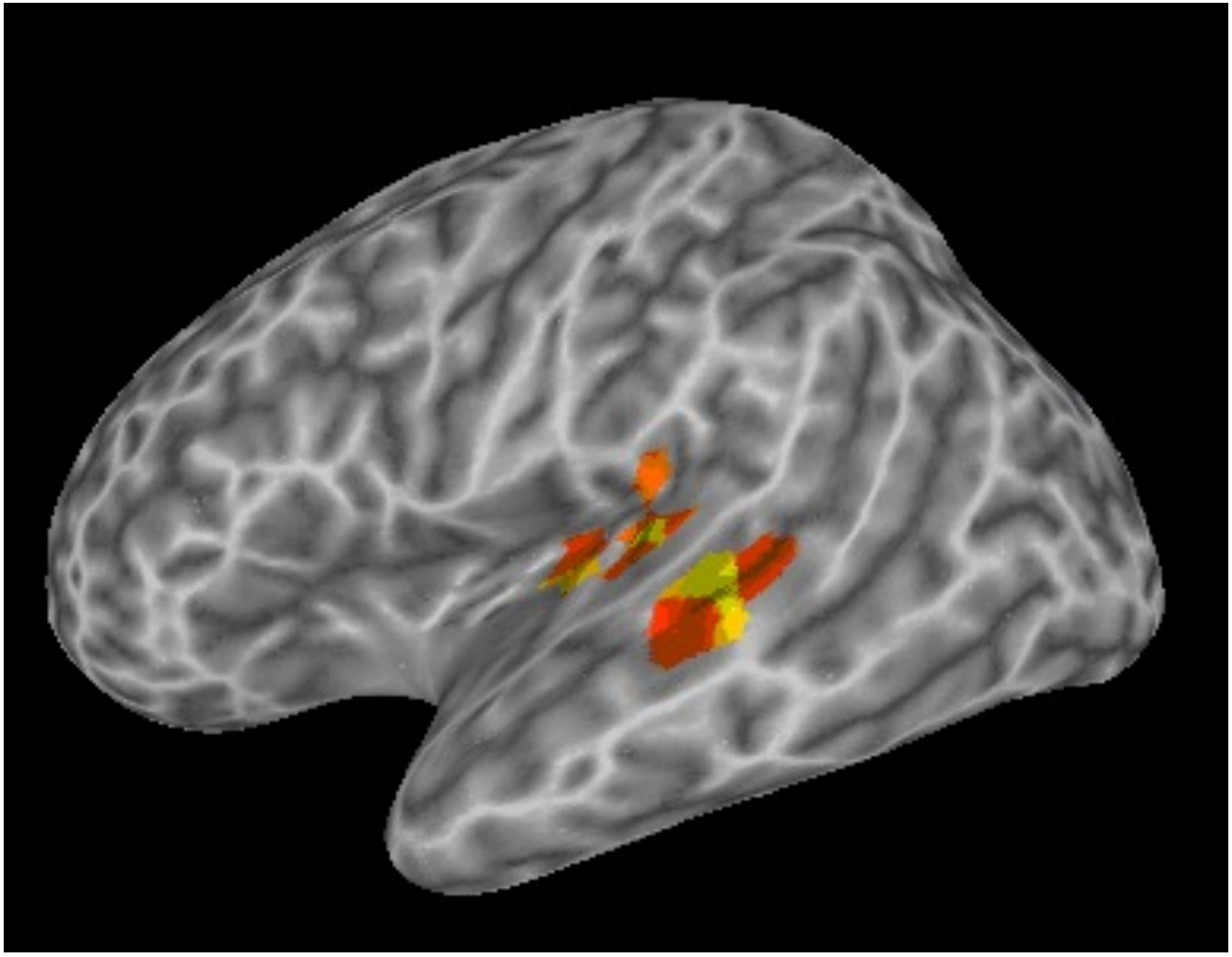
SAM, 500 msec window centered on response, Beta desynchronization



SPM T map 2b>0b {SPM99 t ~ 4.0; $Z_{\equiv}$ ~ 3.10, p ~0.001, k > 10}

Localization not as precise as fMRI, but enhanced temporal resolution. Example from a tone duration experiment



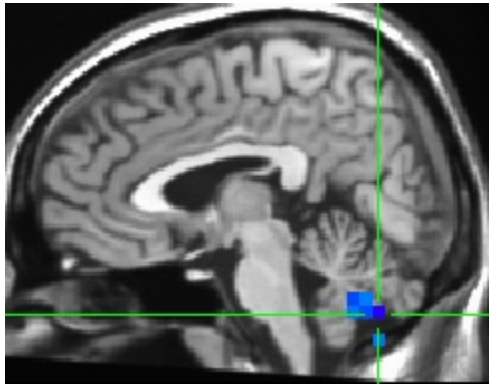


Long non-target tone, < 2s in a loop

Carver et al., 2012

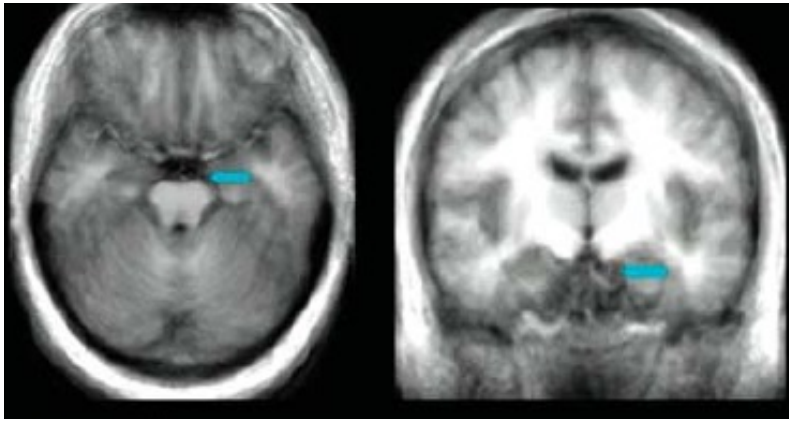
Deep Sources

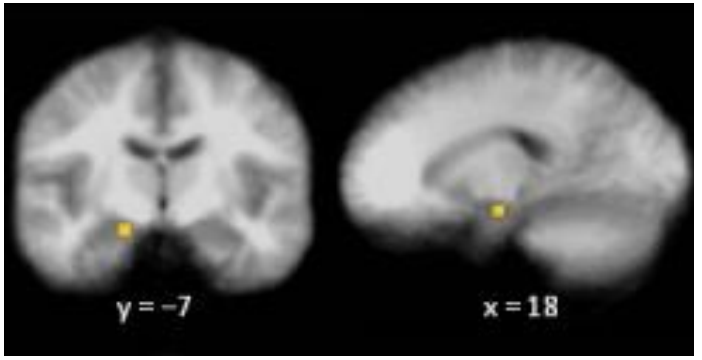
Long deemed to be impossible to observe, but really just a matter of signal-to-noise. Modern MEG systems make it possible.



Cerebellum

Amygdala

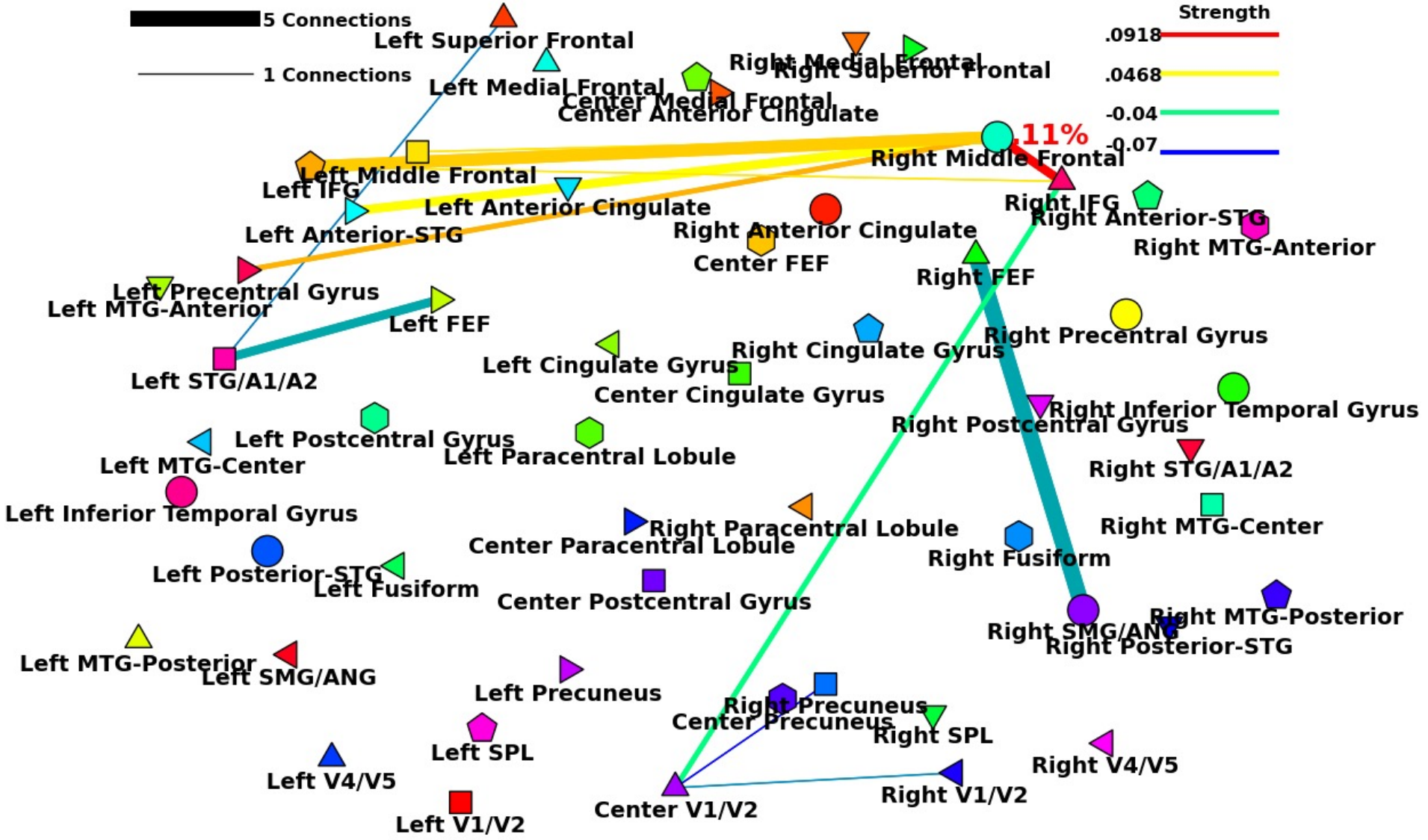




Hippocampus

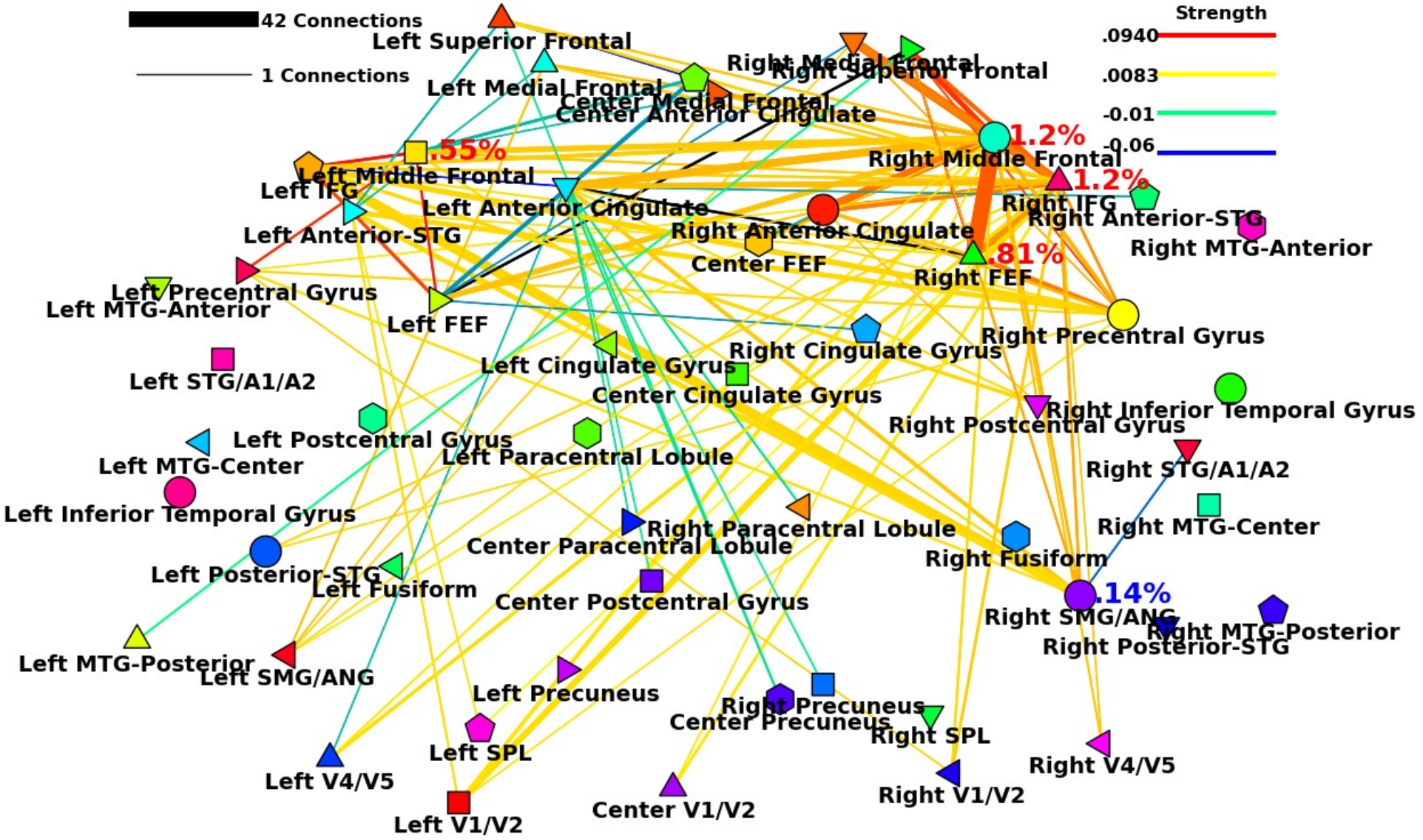
Connectivity?

- as yet no predominant method or theoretical underpinning



Power envelope correlation on virtual channels, N-back

– Tyler Ard dissertation



Coherence, same data

Clinical Research Applications

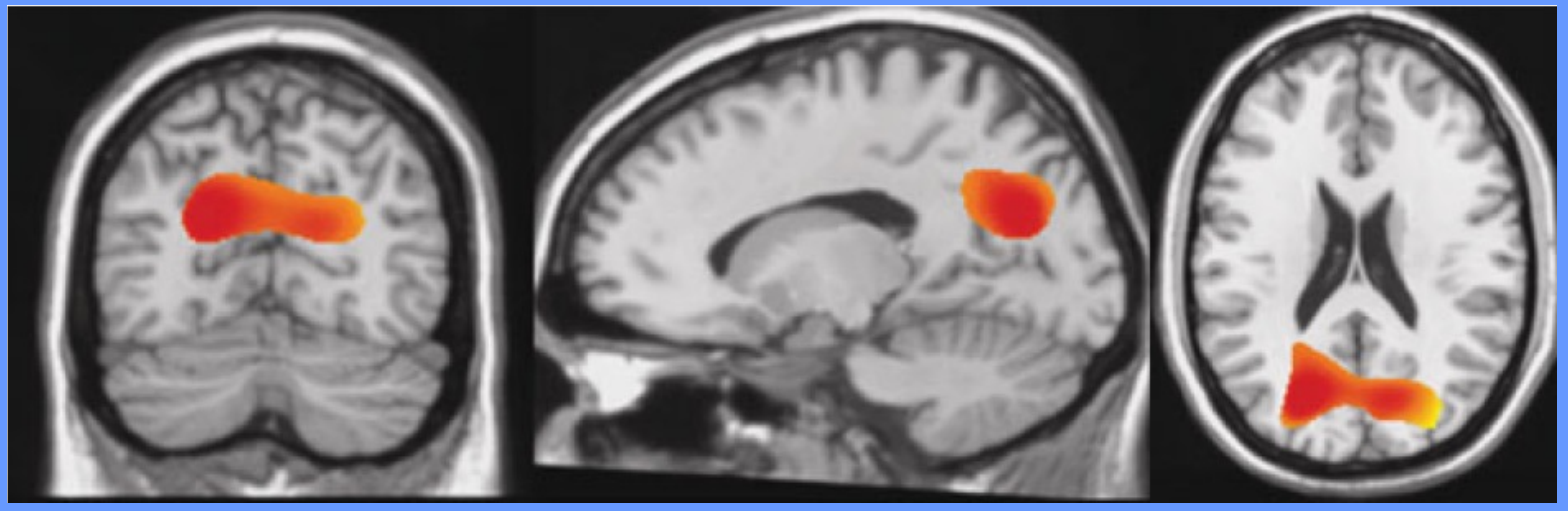
What are the observable signs of altered cortical and subcortical function in MEG?

- Delayed or reduced amplitude evoked responses
- Local oscillatory power changes
- Long range communication differences (conduction delays; lack of synchrony; connectivity patterns)
- Complex measures? (signal-to-noise ratio; entropy)

Evidence for aberrant neuromagnetic activation in patient populations

Magnetoencephalographic Gamma Power Reduction in Patients with Schizophrenia During Resting Condition

Lindsay Rutter,[1] Frederick W. Carver,[1] Tom Holroyd,[1]
Sreenivasan Rajamoni Nadar,[1] Judy Mitchell-Francis,[1] Jose Apud,[2]
Daniel R. Weinberger,[2] and Richard Coppola[1,2]*



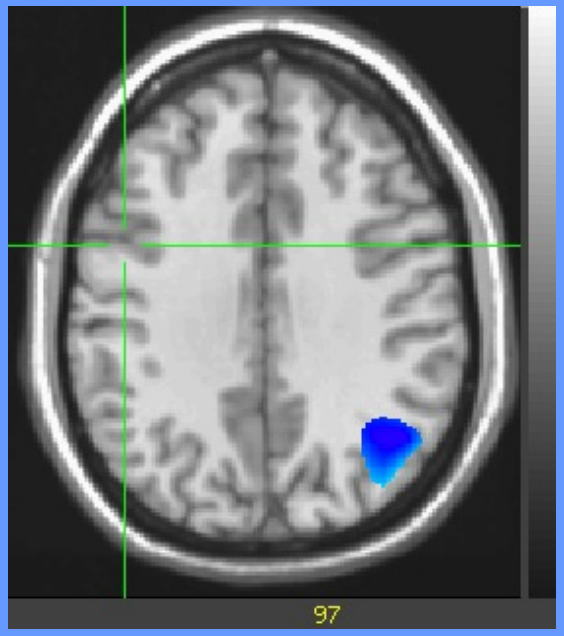
◆ Human Brain Mapping 30:3254–3264 (2009) ◆

Clinical Research Applications

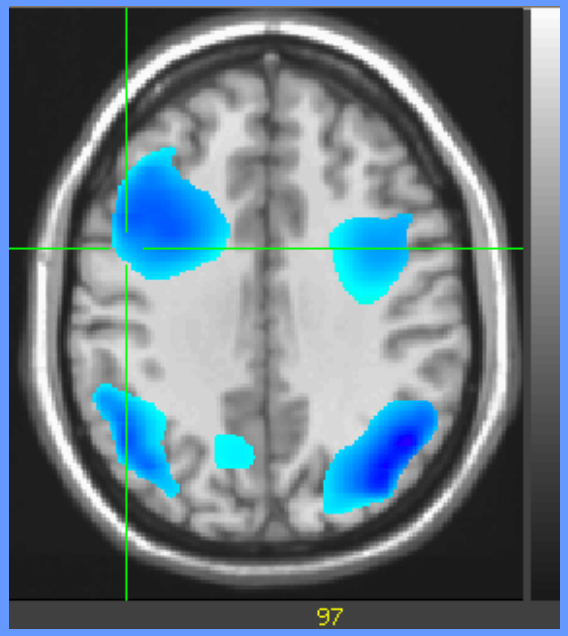
What can be associated with observed differences?

- Genotype / Genetic risk
- Neurotransmitter levels
- Models of network dynamics
- Performance differences / Behavioral phenotypes
- Diagnostic criteria / Symptom severity
- Neuropsychological testing
- Medication / Therapeutic response
- Training / Cortical stimulation

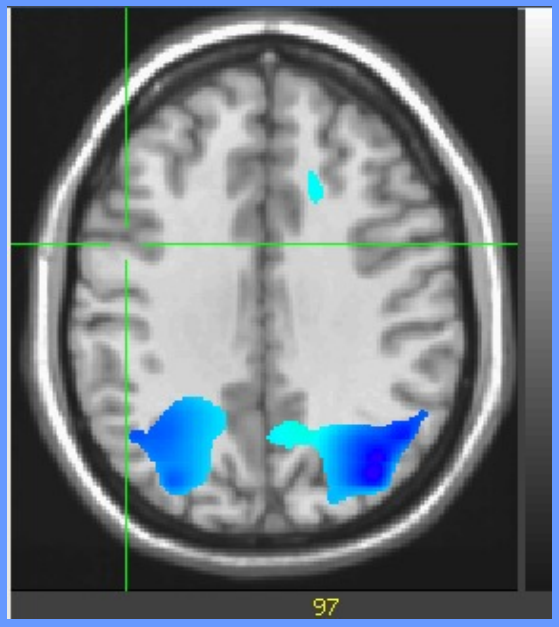
Normal Controls, 2-back activation, beta band



val/val



val/met



met/met

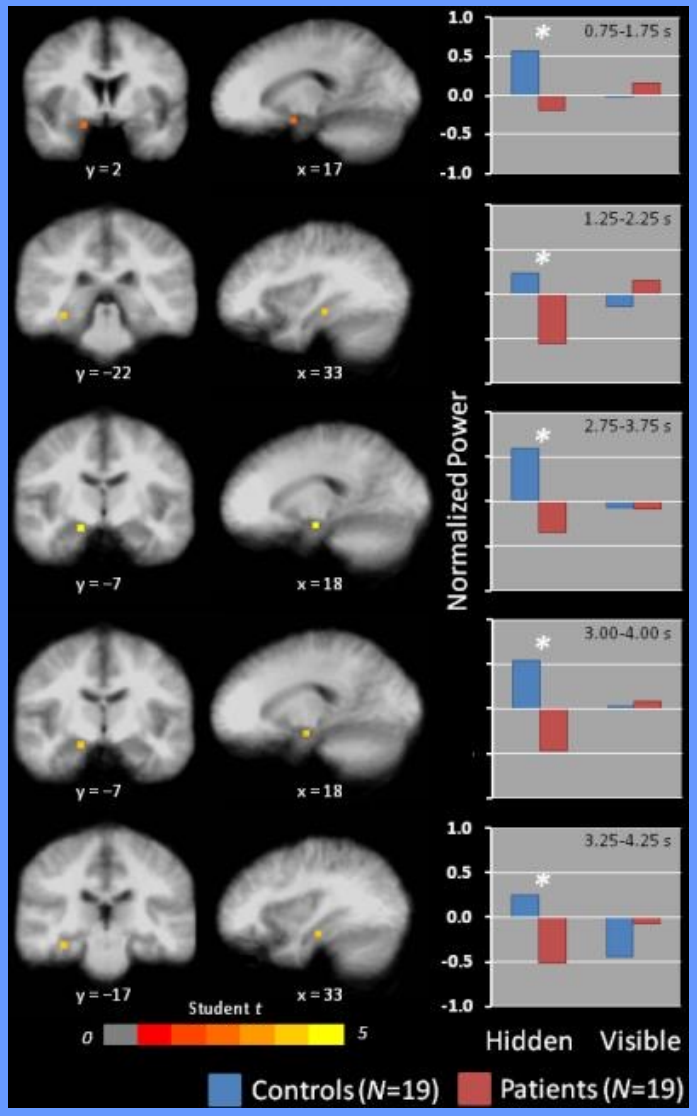
Significant effect of COMT genotype
– involved in dopamine signaling

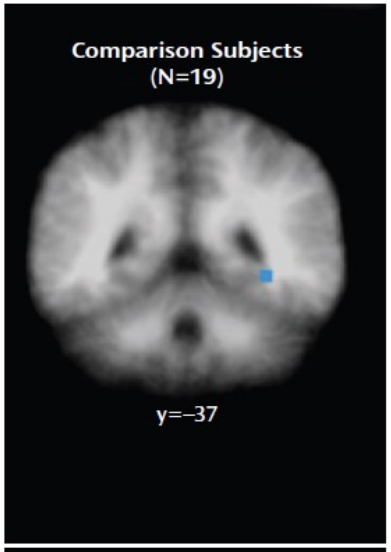
Am J Psychiatry. 2010 Jul;167(7):836-44. Epub 2010 May 3.

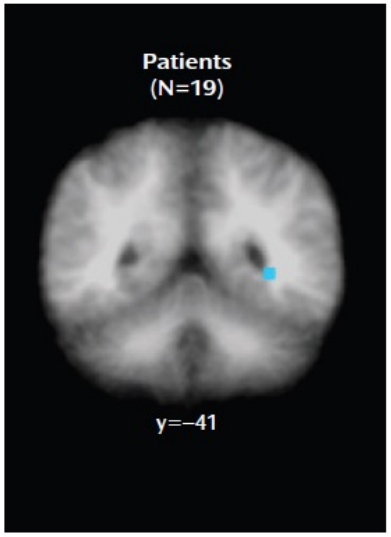
Abnormal hippocampal functioning and impaired spatial navigation in depressed individuals: evidence from whole-head magnetoencephalography.

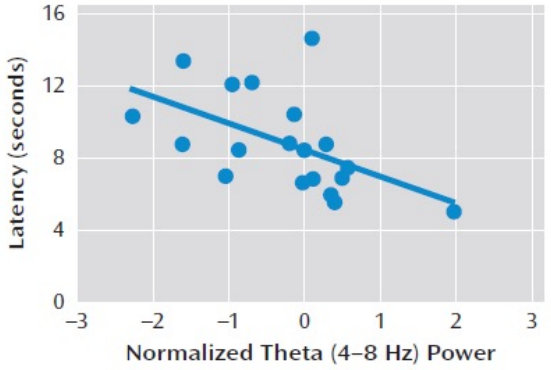
Cornwell BR, Salvadore G, Colon-Rosario V, Latov DR, Holroyd T, Carver FW, Coppola R, Manji HK, Zarate CA Jr, Grillon C.

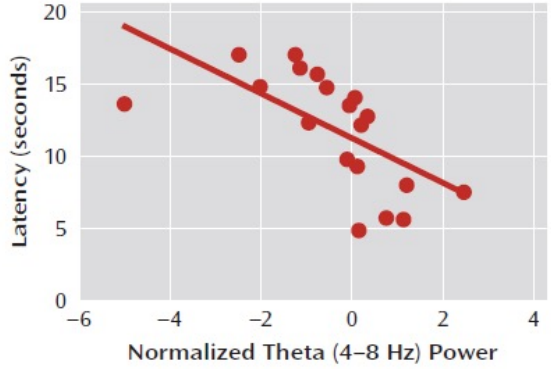
Mood and Anxiety Disorders Program, NIMH, 15K North Dr., MSC 2670, Bethesda, MD 20892, USA. cornwellb@mail.nih.gov





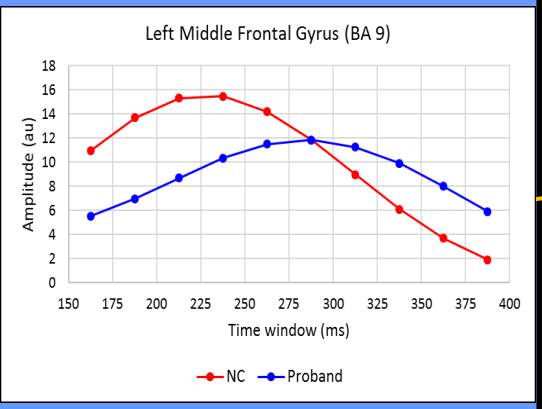


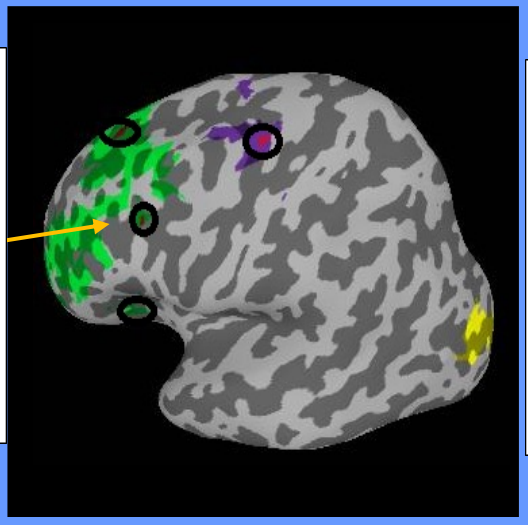


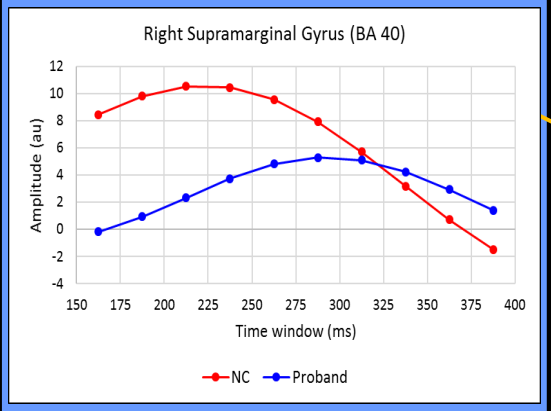


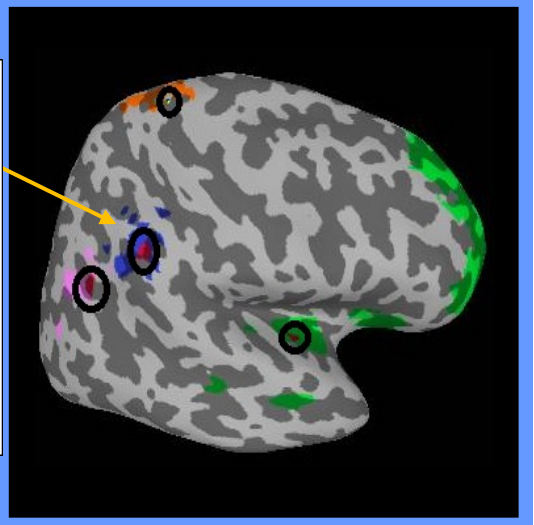
Auditory Oddball P300, Matched sample of 66 patients with schizophrenia and healthy controls

Analysis by Samantha Fradkin, IRTA MEG Core

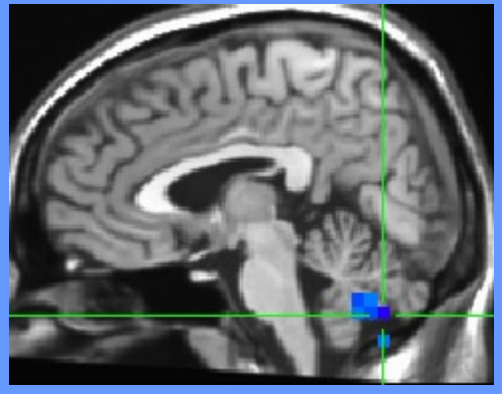




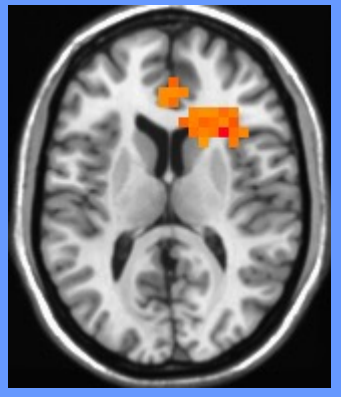




Peak Latency Correlated with IQ and Symptom Scale in Probands



General Intelligence
'Big-G' Dickinson CTNB



Suspiciousness
Subscale from PANSS

MEG and Pharmaceutical Response

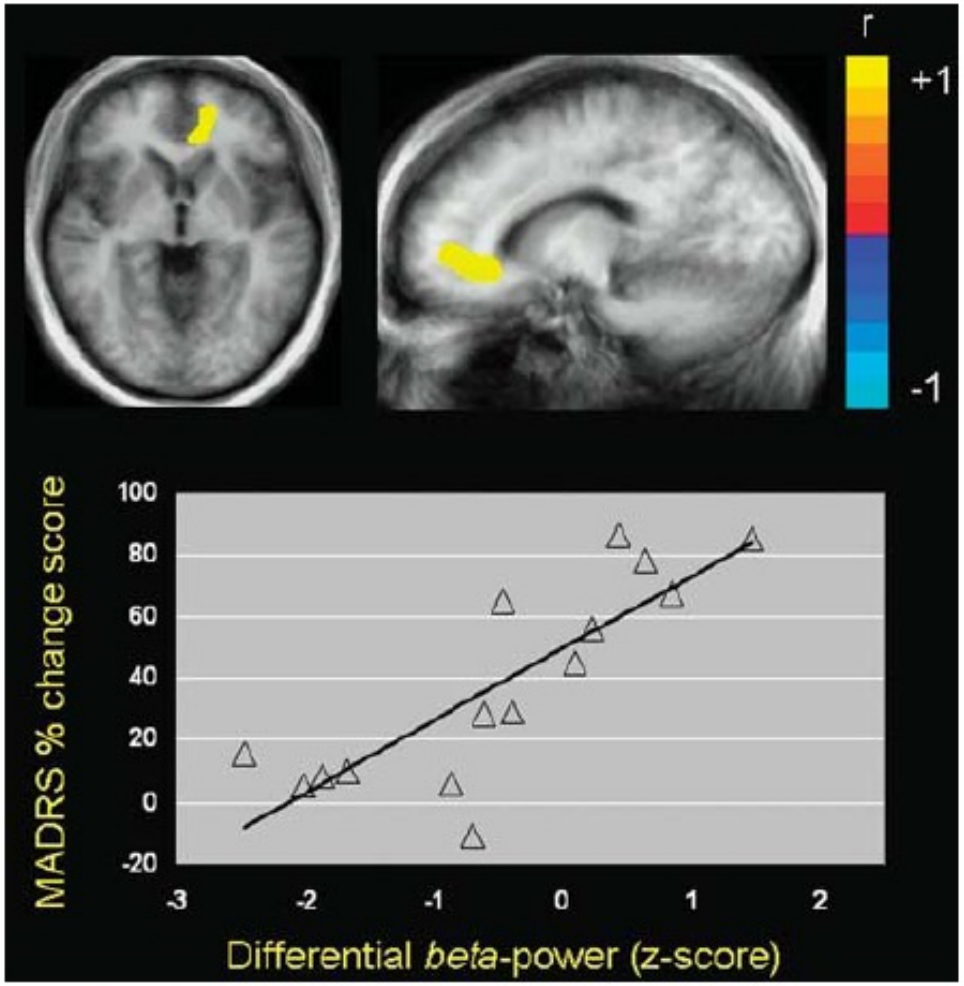


Figure 1 Pearson correlation between beta desynchronization in the anterior cingulate cortex (ACC) and change in depressive symptoms 230 min after ketamine infusion for the 2-back *vs* 1-back comparison in patients with MDD (ACC peak: $x = -15$, $y = 45$, $z = -1$ mm; coordinates expressed according to the stereotaxic atlas of Talairach and Tournoux (Talairach and Tournoux, 1988)). These coordinates localize to the pregenual portion of the ACC, although the cluster of voxel *t*-values

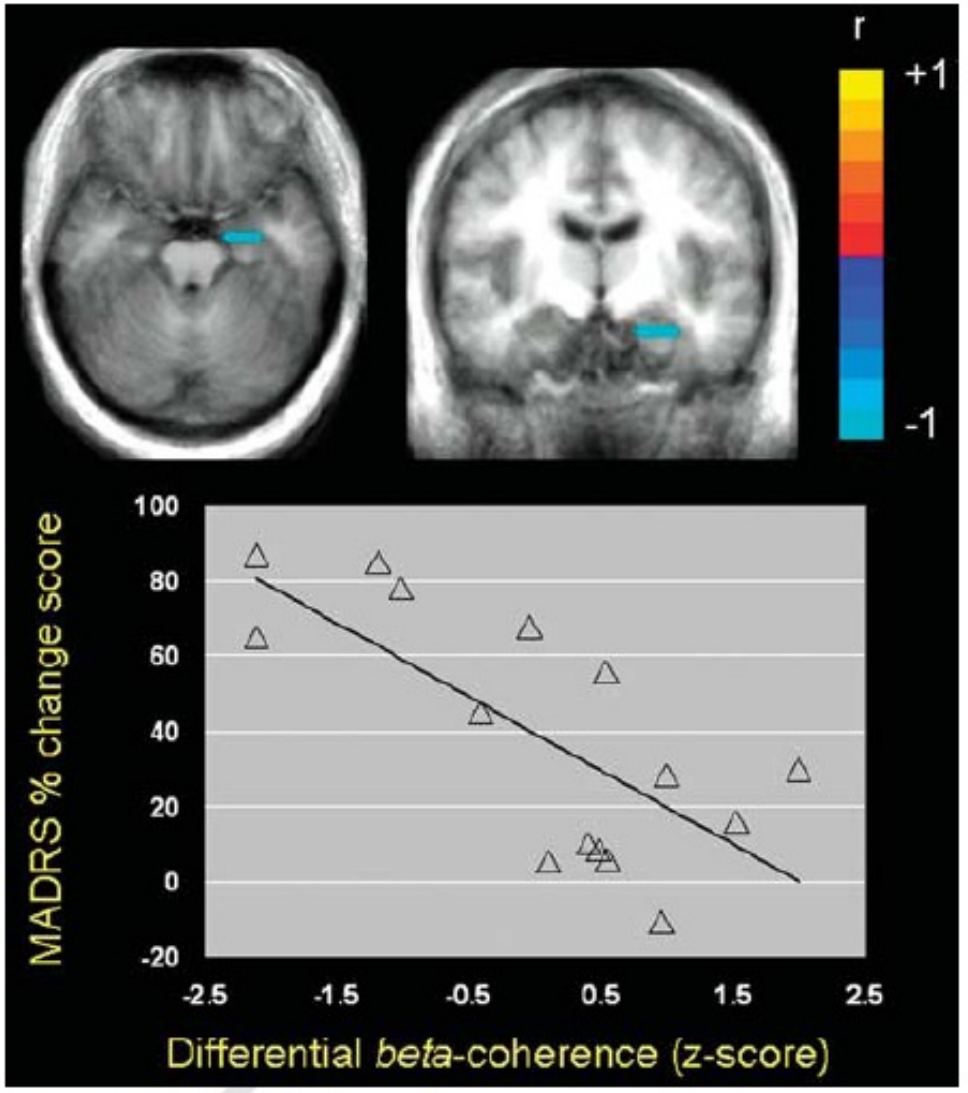


Figure 2 Pearson correlation between differential source coherence of the pgACC with the left amygdala and change in depressive symptoms 230 min after ketamine infusion for the 2-back *vs* 1-back comparison in patients with MDD (left amygdala peak: $x = -30$, $y = -7$, $z = -16$ mm;

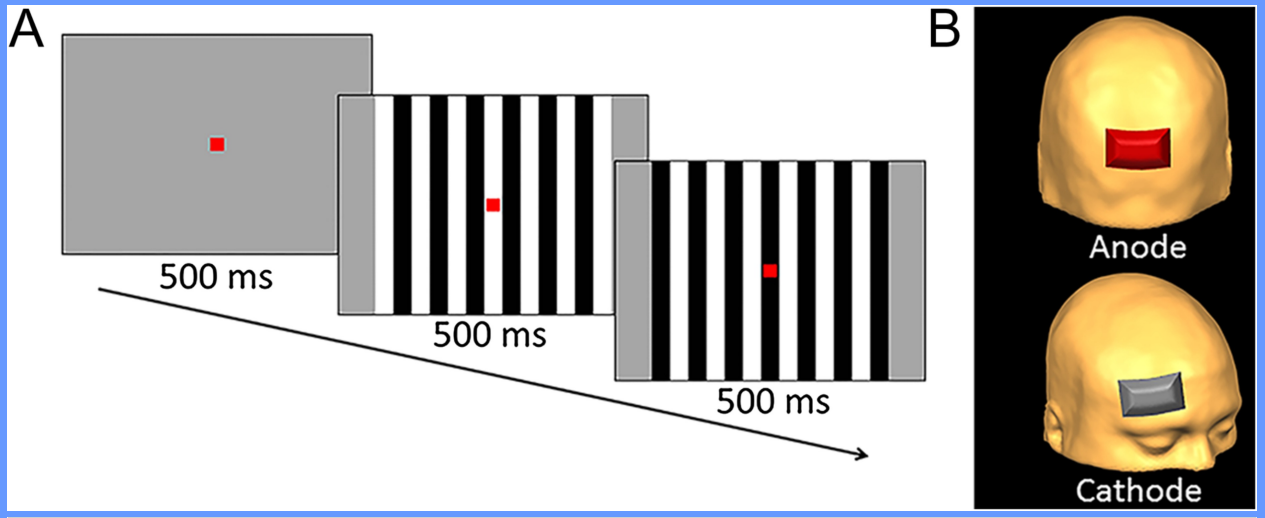
Anterior Cingulate Desynchronization and Functional Connectivity with the Amygdala During a Working Memory Task Predict Rapid Antidepressant Response to Ketamine

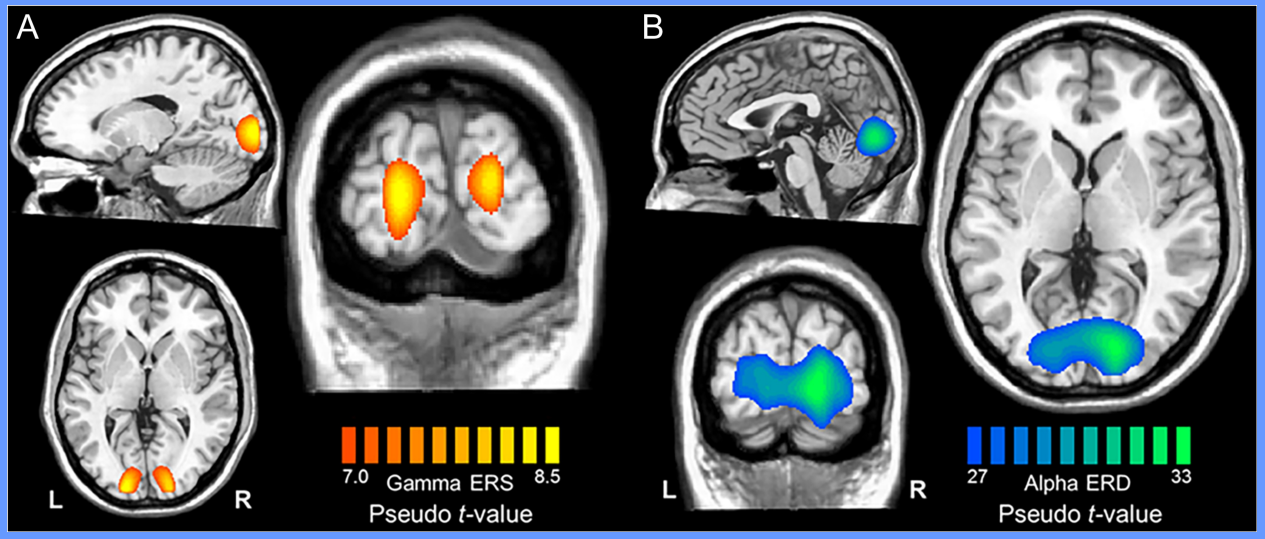
Giacomo Salvadore*[1,2], Brian R Cornwell[2], Fabio Sambataro[3], David Latov[1,2], Veronica Colon-Rosario[1], Frederick Carver[4], Tom Holroyd[4], Nancy Diaz-Granados[1,2], Rodrigo Machado-Vieira[1,2], Christian Grillon[2], Wayne C Drevets[2] and Carlos A Zarate, Jr[1,2]

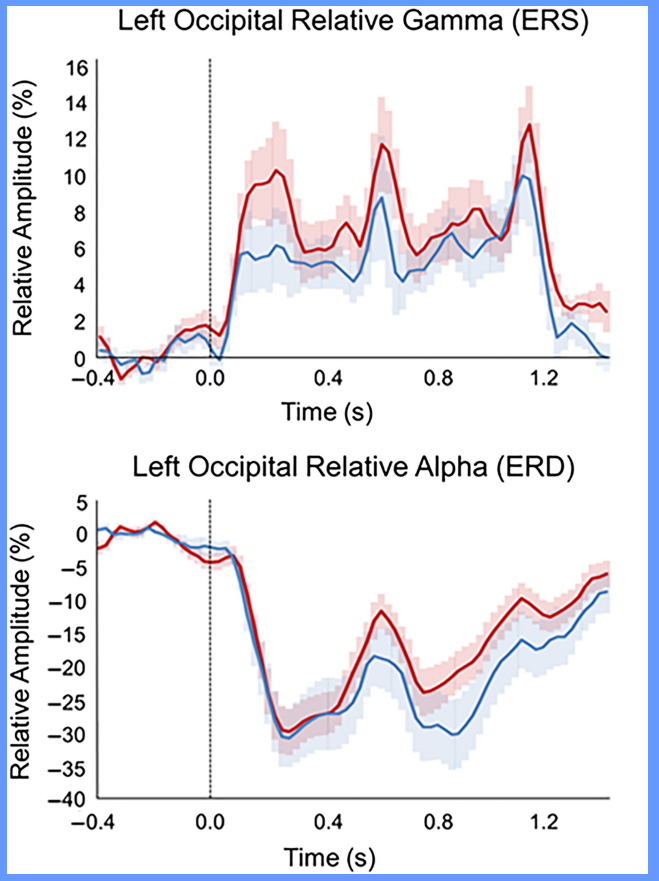
Neuropsychopharmacology (2010), 1–8

tDCS Modulates Visual Gamma Oscillations and Basal Alpha Activity in Occipital Cortices: Evidence from MEG.

Wilson TW, McDermott TJ, Mills MS, Coolidge NM, Heinrichs-Graham E.
Cereb Cortex. 2018 May 1;28(5):1597-1609.





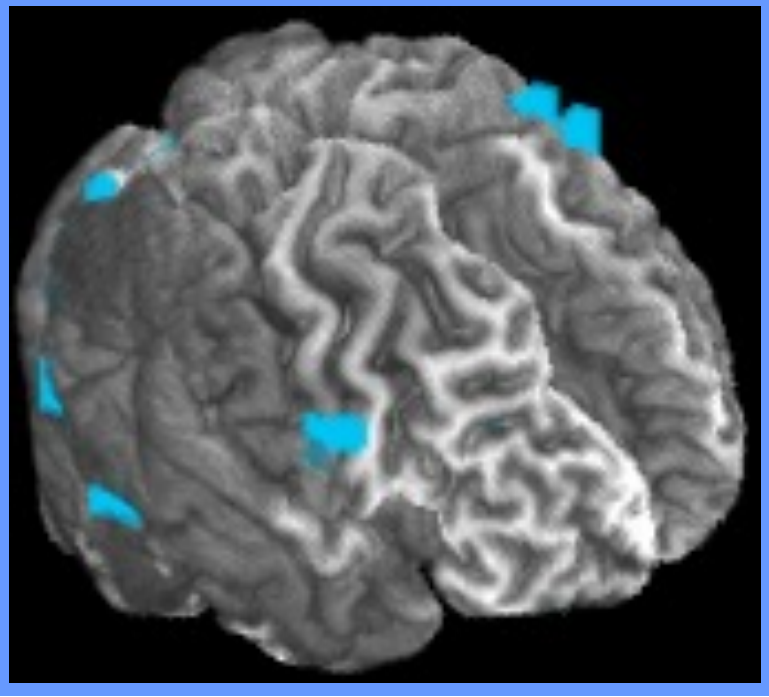


Targeted cortical reorganization via brain-computer interface (BCI) training in chronic stroke.

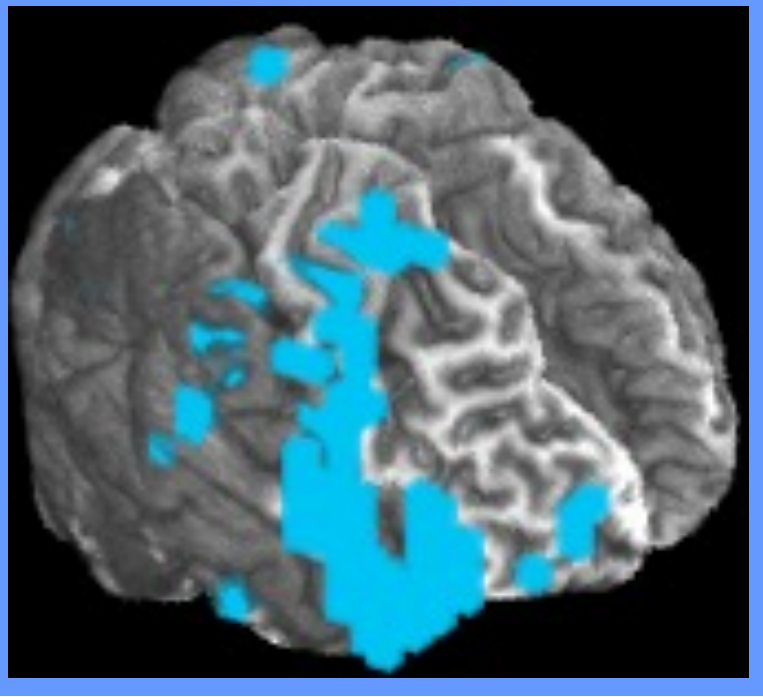
TD Ard, ER Buch, C Weber, AD Fourkas, N Birbaumer, LG Cohen

Human Cortical Physiology Section and Stroke Neurorehabilitation Clinic, NINDS
Inst of Medical Psychology and Behavioral Neurobiology, Univ of Tubingen, GERMANY

Patient Before Training



Patient After Training



The future?

NeuroImage

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A new generation of magnetoencephalography: Room temperature measurements using optically-pumped magnetometers

Elena Boto [a, 1], Sofie S. Meyer [b, 1], Vishal Shah [c], Orang Alem [c], Svenja Knappe [c], Peter Kruger [d], T. Mark Fromhold [d], Mark Lim [e], Paul M. Glover [a], Peter G. Morris [a], Richard Bowtell [a, 1], Gareth R. Barnes [b, 1], Matthew J. Brookes [a] [1] ✉

OPMs measure the transmission of laser light
through a vapour of spin-polarised rubidium atoms

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