Deep Sources

and other things you aren't supposed to see with MEG

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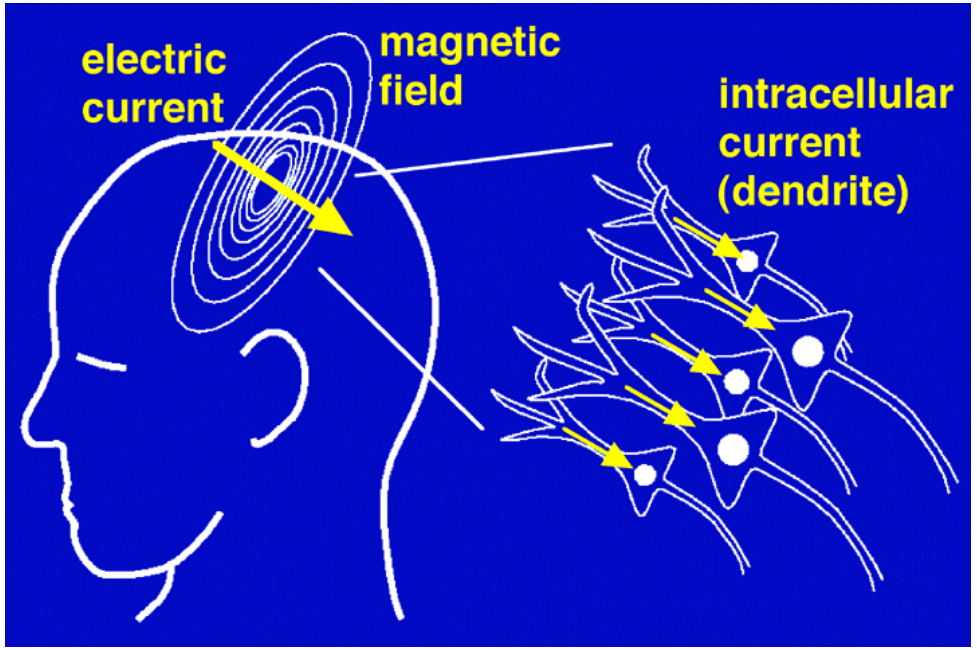
Deep Sources Can't Be SEEN

- Not True; Difficult but possible
- Yet many still believe we can't see them, including textbooks
- Why does this idea persist, despite many papers to the contrary?
- Reasons why people think this: presented as *logical fallacies*
  - Anatomical – Theoretical
  - Contrast with EEG
  - Different MEG technologies
    - Difference between systems
    - Old technology had issues
  - Analysis methods have improved

Anatomy

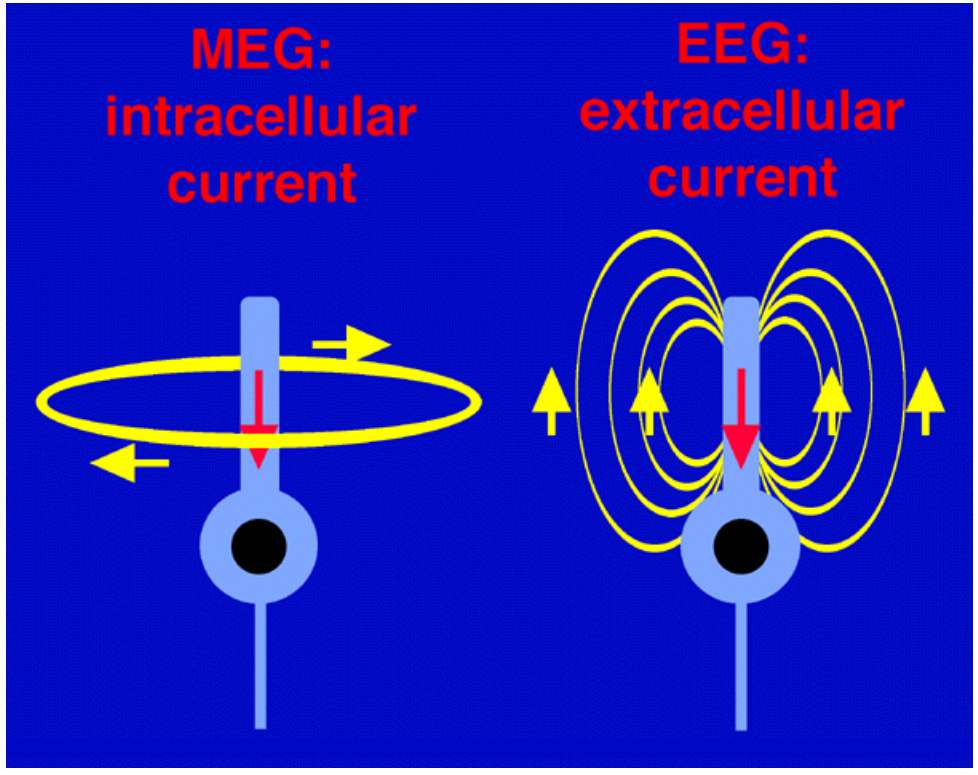
- Theoretical source of MEG signal leads to *fallacy of the inverse*
- Parallel apical dendrites of cortical pyramidal cells assumed to generate strong MEG. Modelled as a ‘dipole’, a point source of current
- But ‘if A then B’ doesn’t mean ‘if B then A’



Exaggerated Contrast with EEG

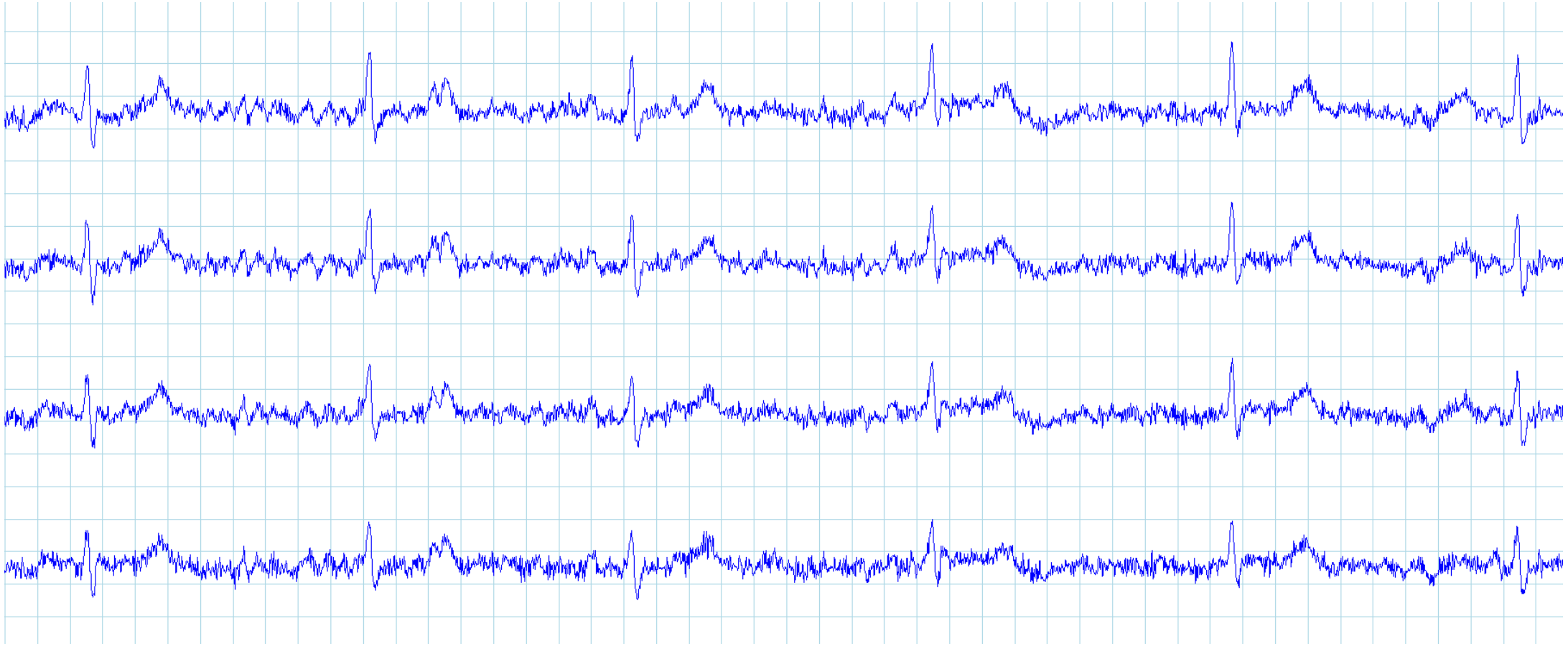
- Differences lead to *false dichotomy*
- Trade off at depth: more signal w/ EEG, but also harder to localize
- Really a Signal/Noise issue in MEG: can be overcome w/ modern tech. and better analysis

MEG
field strength / radius^2



EEG
electric signal
distorted by
surrounding tissue

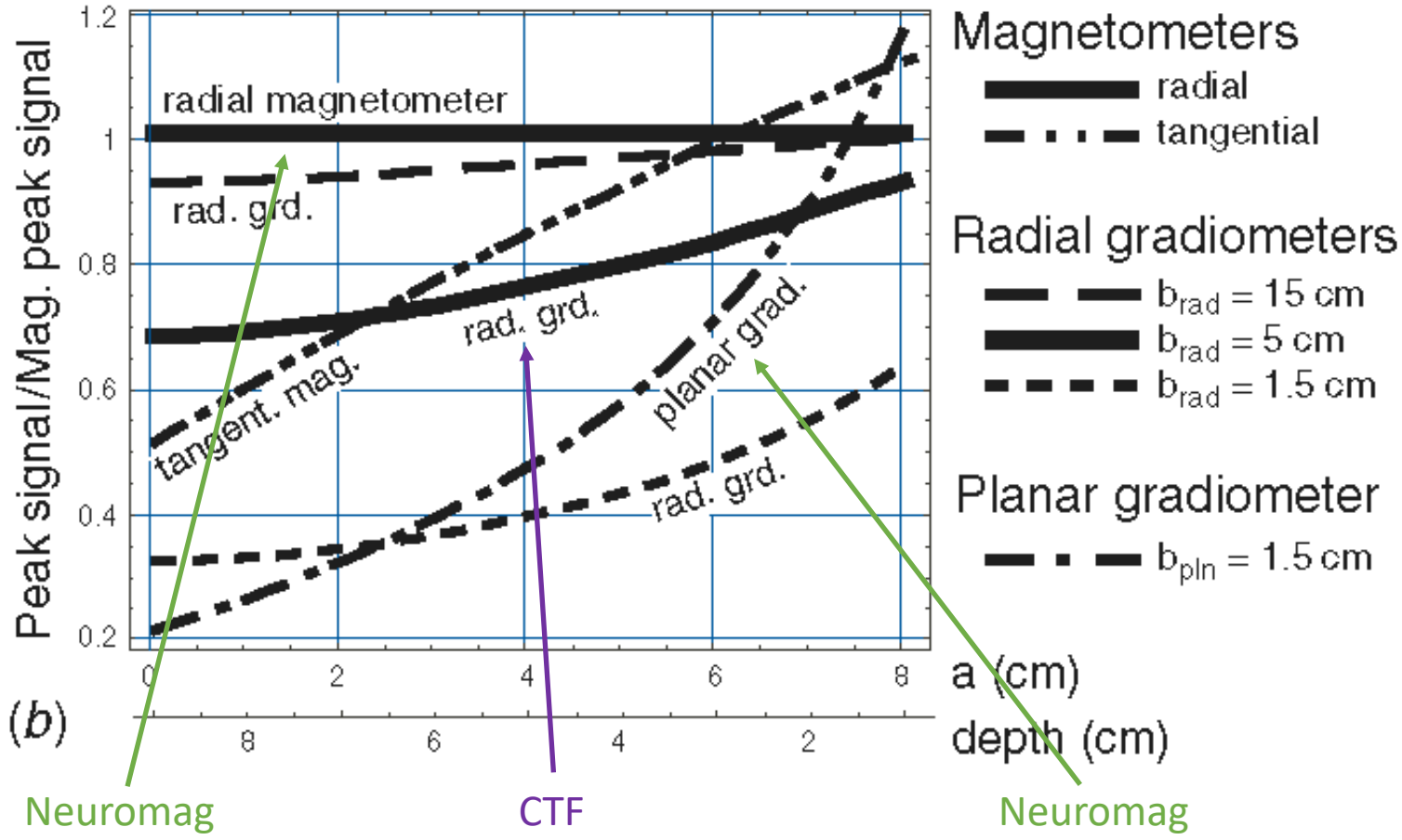
- Strong Signal, Deep Source, Heart Beat



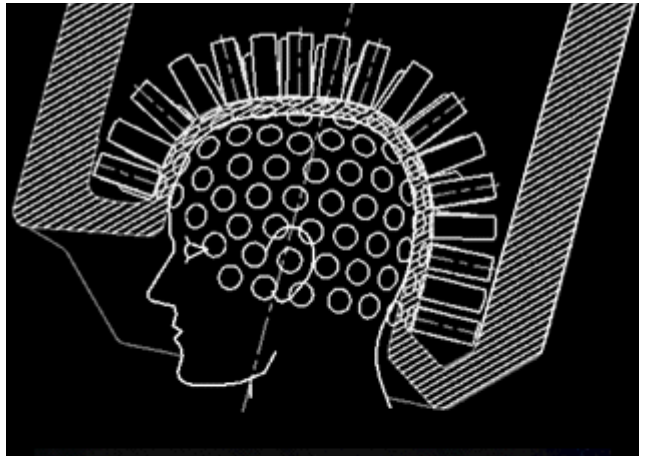
Technological Differences

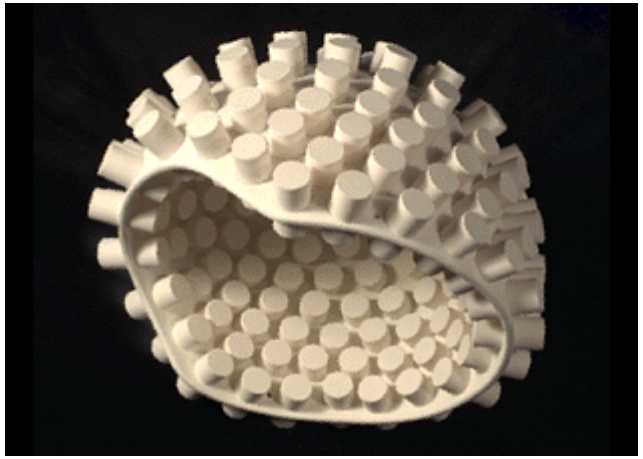
- Gradiometer: CTF vs. Neuromag creates *false equivalence*
- CTF Gradiometer can see deeper

Vrba & Robinson, 2002



- Technological development – less noise, more channels
  - Our system has 275 channel whole head coverage
  - Early systems had 7 or fewer in one location
  - System placed in magnetically shielded room
  - 30 reference sensors subtract common noise

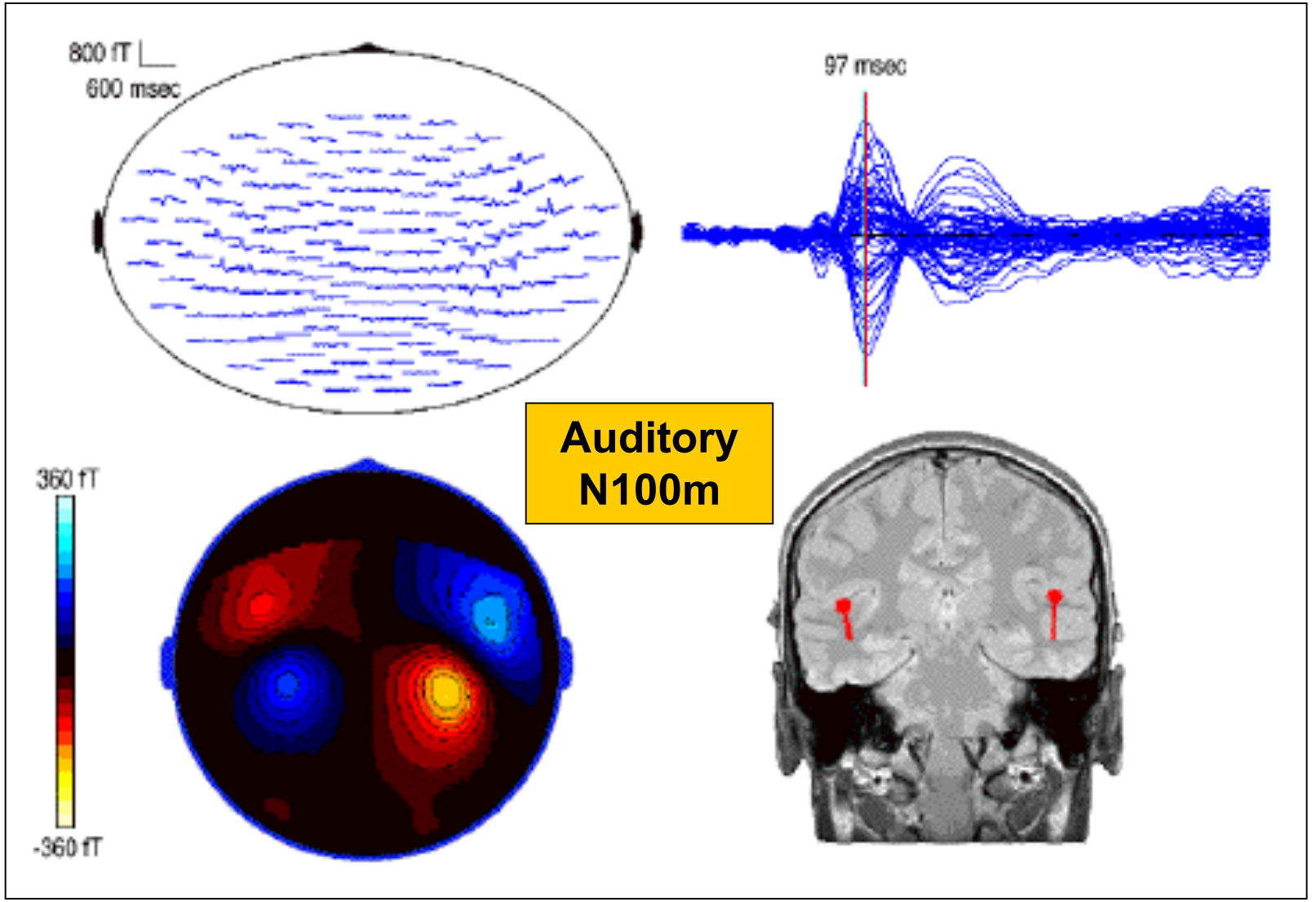




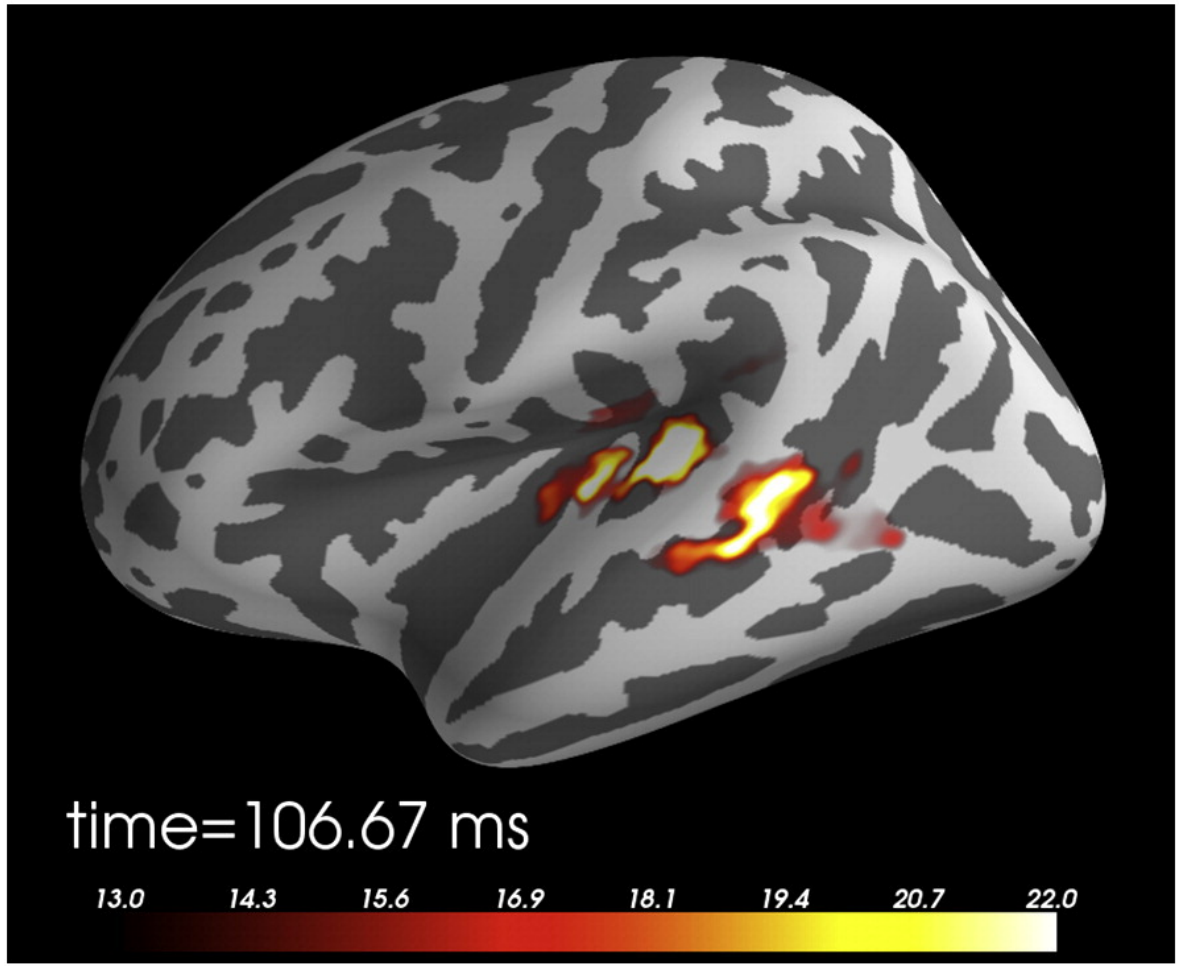
Analysis Methods

- Early methods either assumed a cortical source, or they could only see strongest of multiple sources, thus *argument from ignorance*
- Earliest: Dipole Fit, finds only one or two of strongest sources
- Minimum Norm Estimate (MNE) developed for Neuromag, assumes cortical source
- Beamforming (aka SAM) overcomes issues of older methods
  - A unique spatial filter for each voxel blocks noise/activity from elsewhere
  - Limiting search to frequency bands of activation further reduces complexity
  - Contrasting power in bands between conditions isolates task related activity
  - Successfully images deep sources but has difficulty near center (e.g. thalamus) and with highly synchronous sources

Dipole Fit



MNE



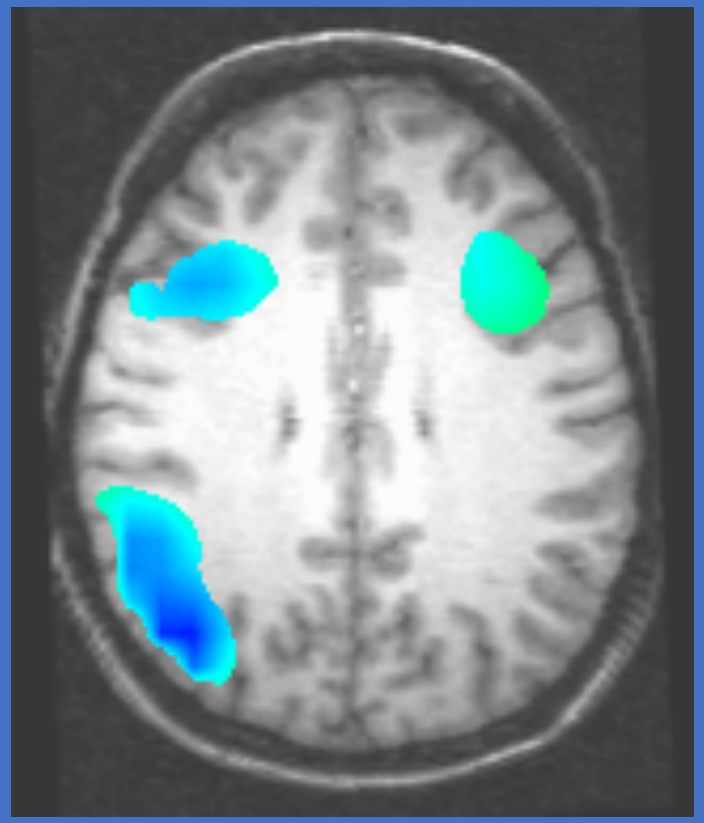
SAM

Spatial filter at each voxel blocks outside activity

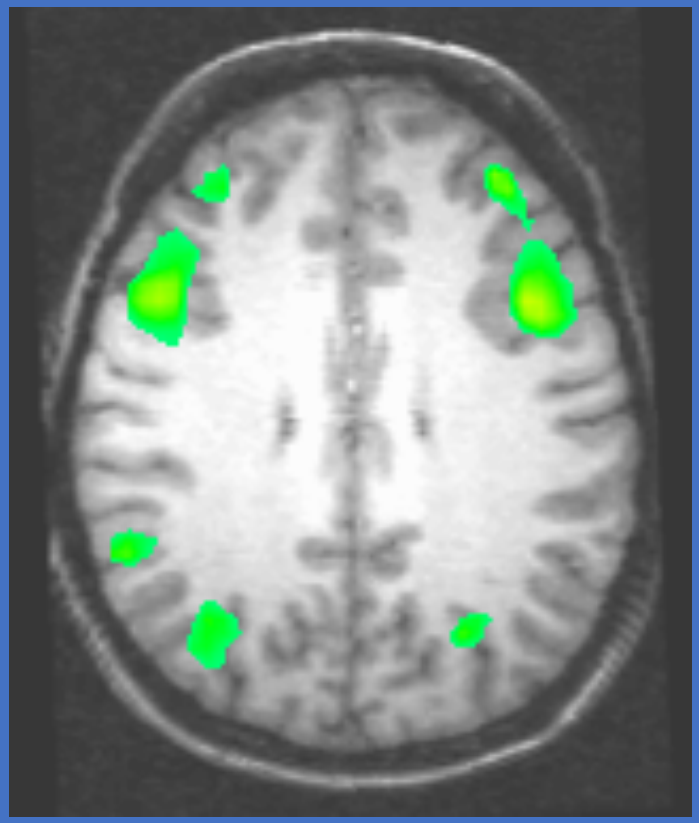
Each voxel is a contrast of two conditions, so the source strength doesn't matter as long as there is a difference between conditions.
e.g. log(A/C)

MEG and fMRI

2-back vs 0-back, same 12 subjects



SAM 500ms window centered on response, Beta desynchronization



SPM T map 2b>0b

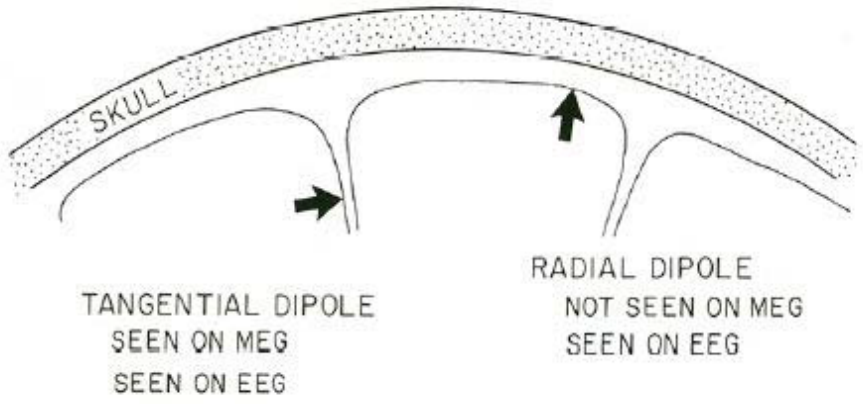
CTNB and NIMH MEG Core

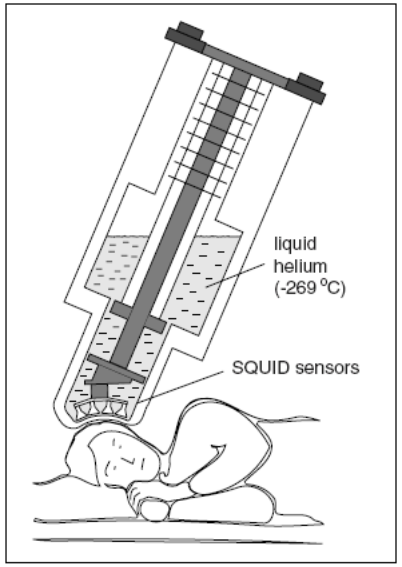
Other things you *can't* see: again, difficult but not impossible

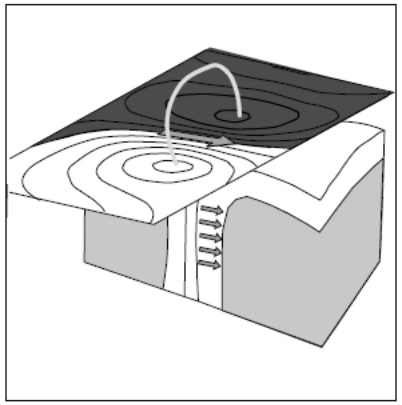
- Radially oriented sources
- Anatomy causes source cancellation
- Lack of parallel fibers means no net current
- Neuronal spiking

Can only see sources tangential to skull: *Causal Oversimplification*

- Again, used in contrast with EEG
- Would mean MEG can only see sulci
- But, old technology had limited head coverage
- Field from any orientation will escape head somewhere



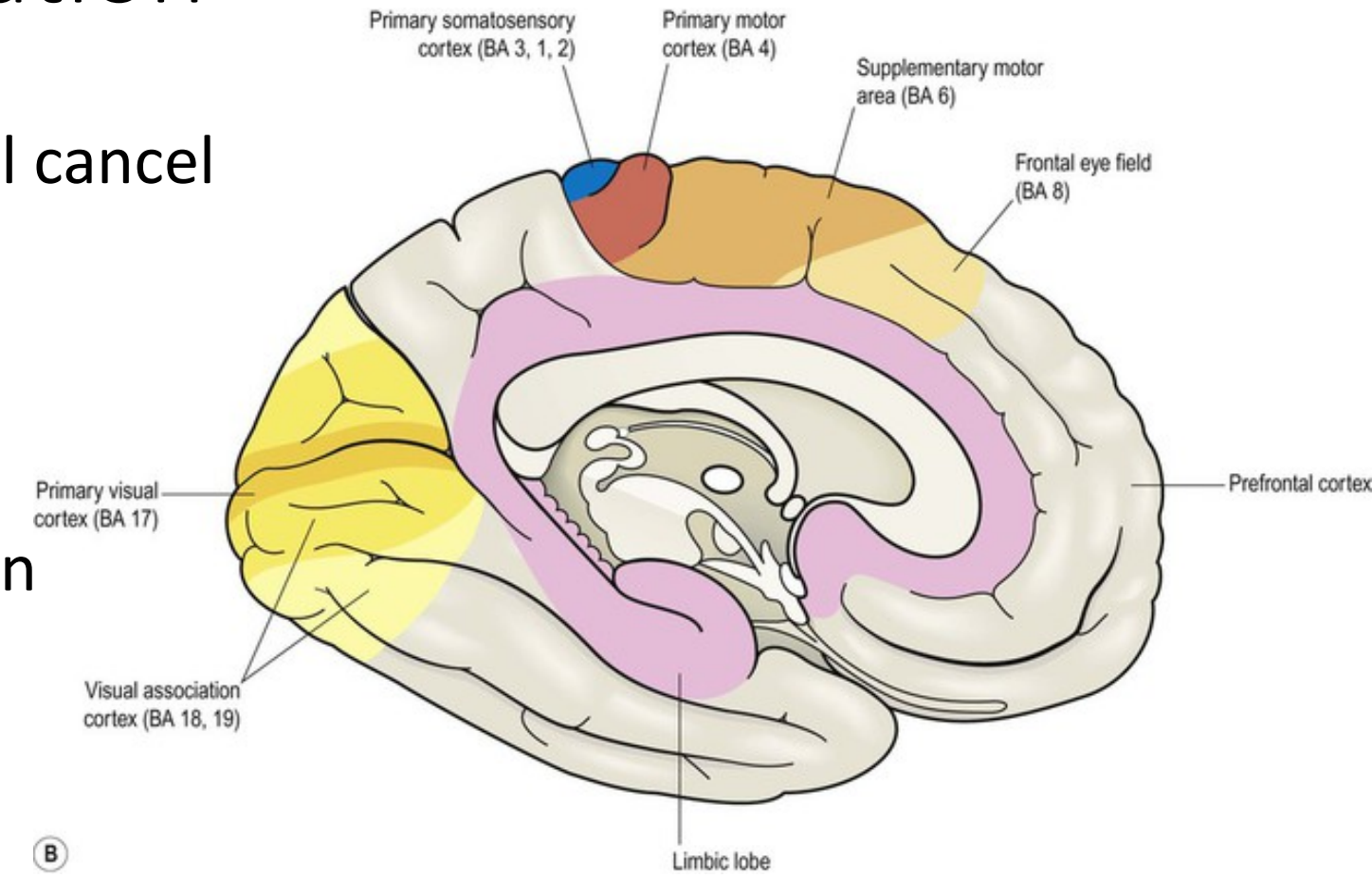




Anatomical Cancellation

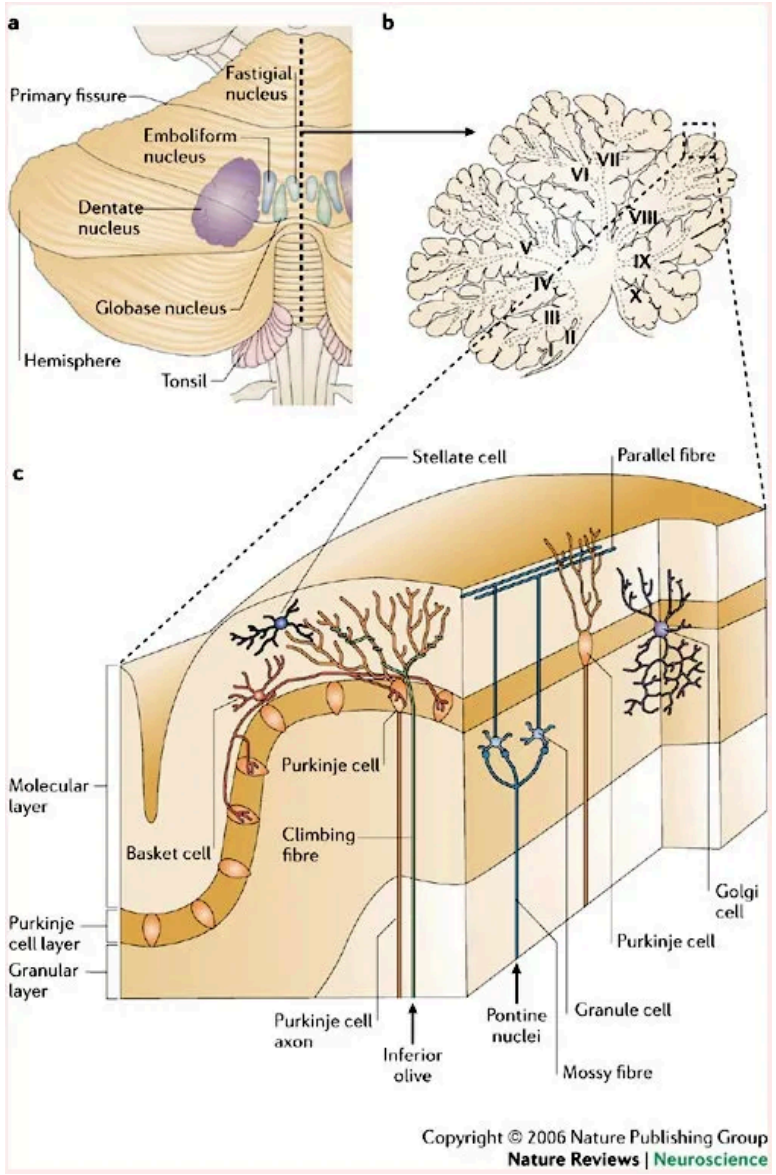
- Dipoles facing each other will cancel

- Bilateral cortical midline →
- Cerebral/Cerebellar sulci
- But never perfect cancellation



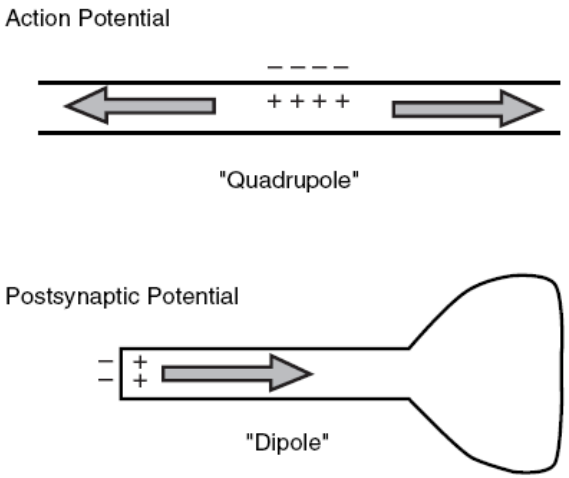
Lack of columnar dendrites

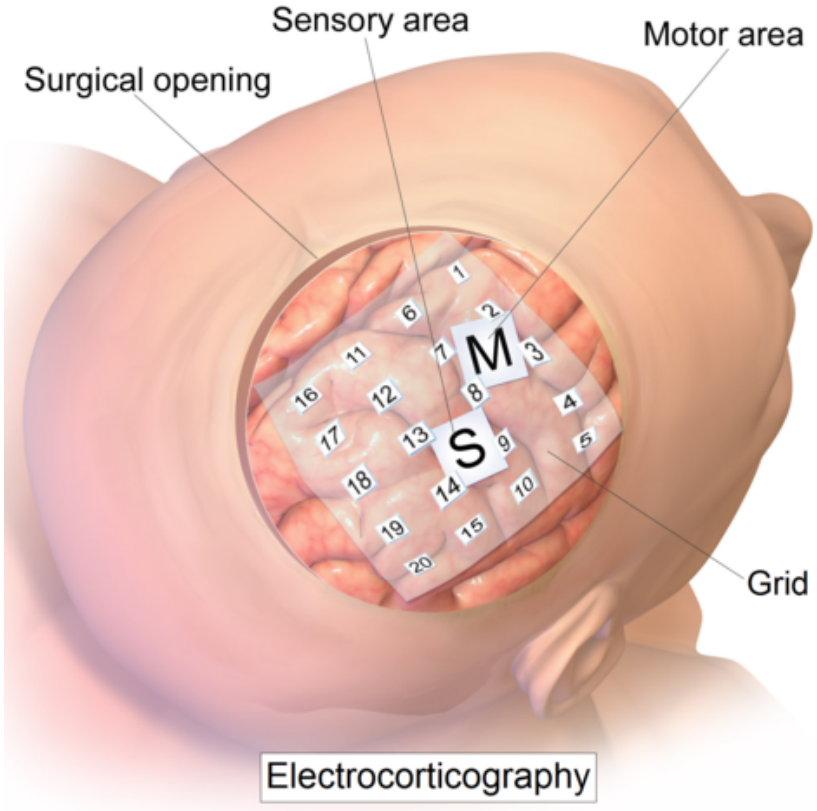
- Amygdala
- Cerebellum →
- But orientations never perfectly random



Neuronal Spiking

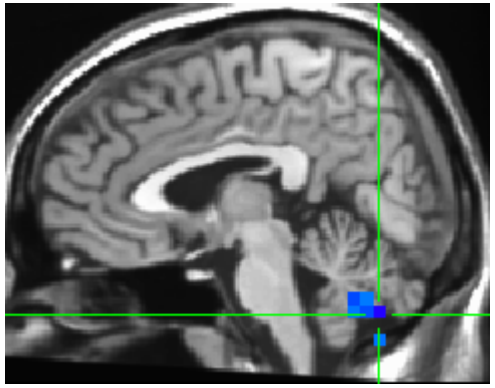
- Seen in ECoG as broad band high gamma activity
- Axonal activity should cancel before reaching MEG sensors
- But maybe not…

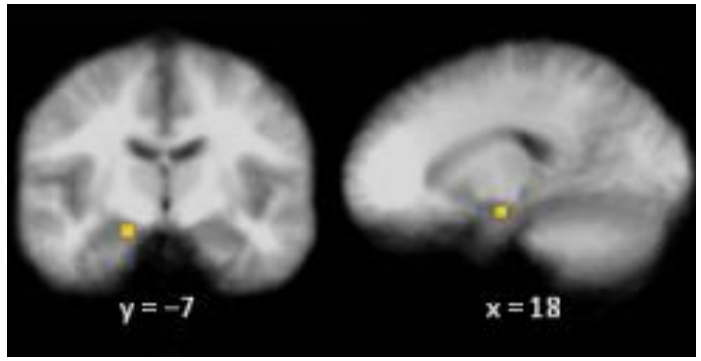


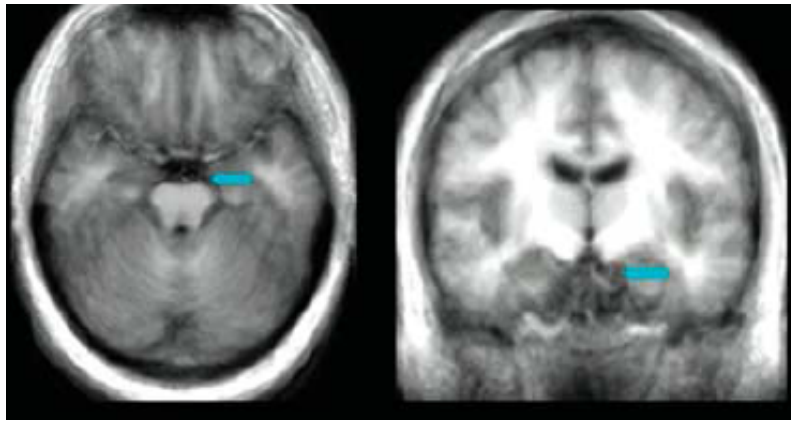


Examples from NIH MEG Researchers

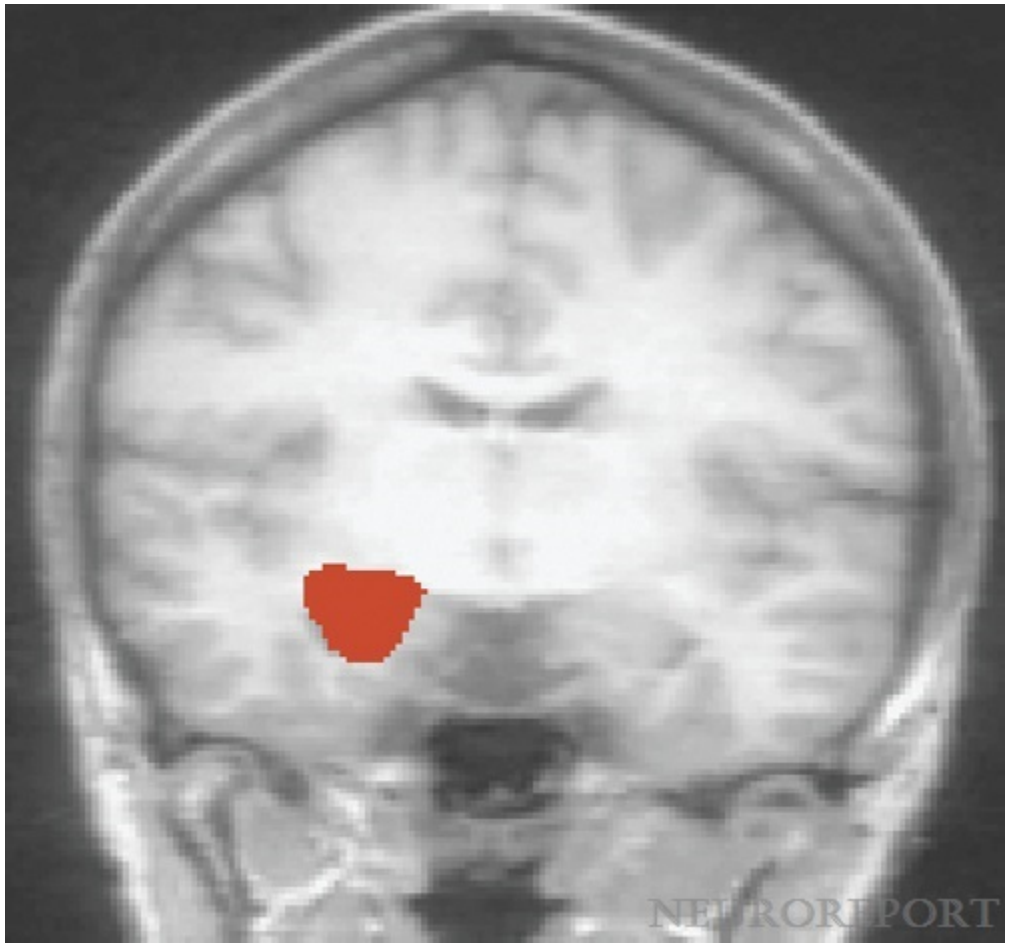
- Amygdala
- Hippocampus
- Basal Ganglia
- Cerebellum
- High Gamma





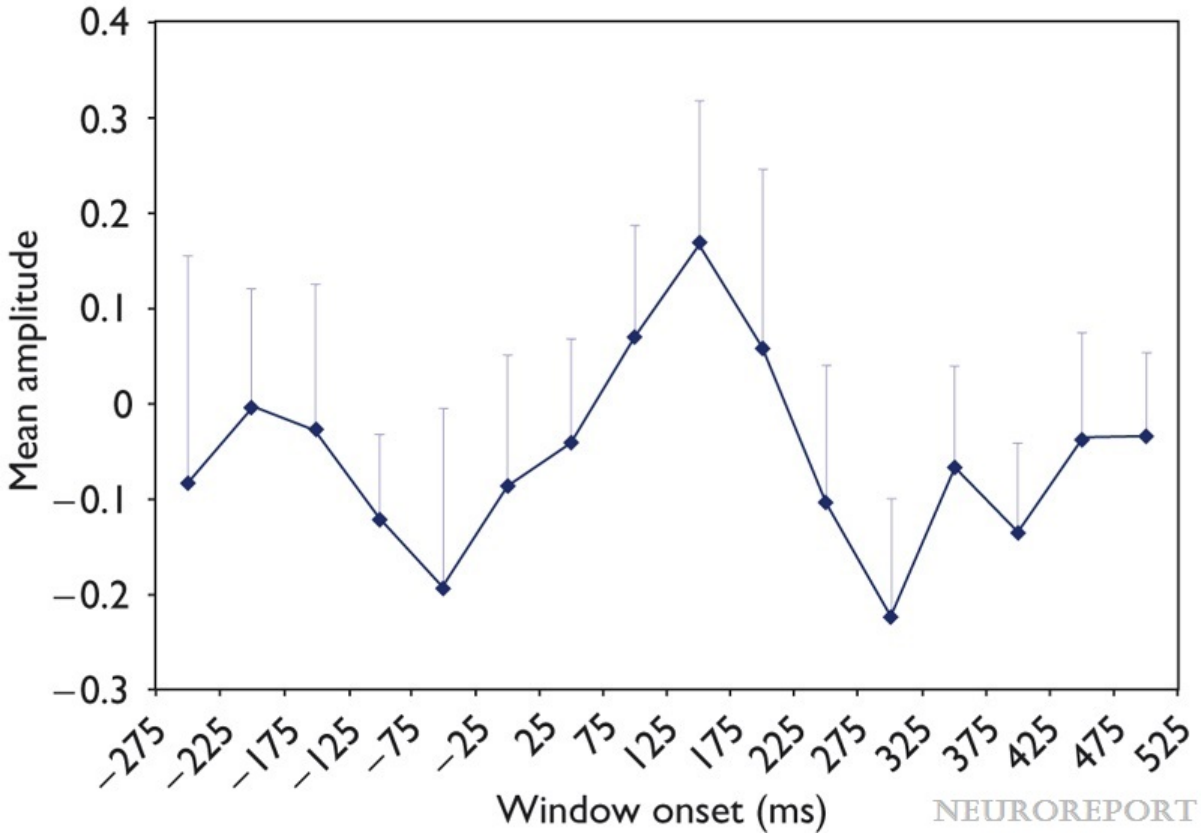


Amygdala



Amygdala peaks 150ms after negative word

- **Amygdala activation in affective priming: a magnetoencephalogram study**
- Garolera, Maite; Coppola, Richard; Muñoz, Karen E.; Elvevåg, Brita; Carver, Frederick W.; Weinberger, Daniel R.; Goldberg, Terry E.
- NeuroReport18(14):1449-1453, September 17th, 2007.



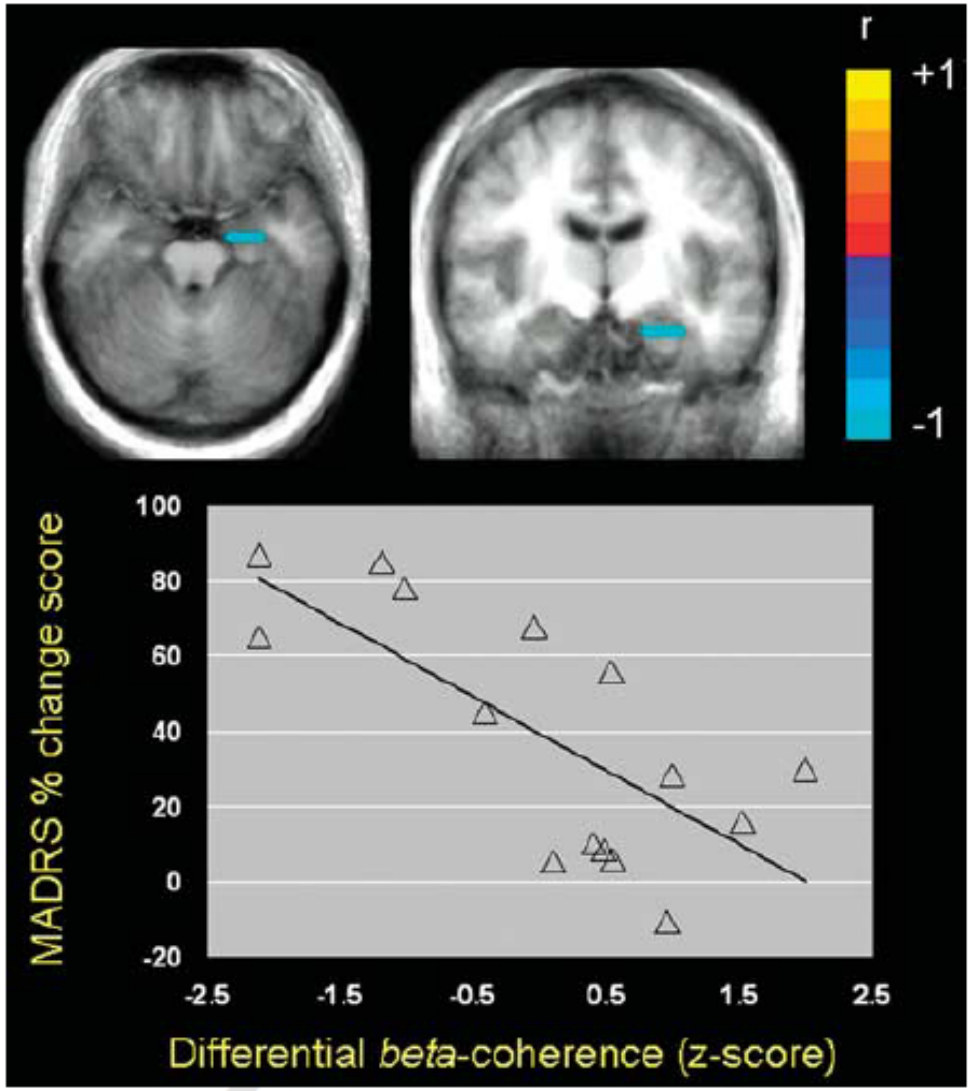
Amygdala

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

Coherence between amygdala and ACC predicts antidepressant response to ketamine



Hippocampus

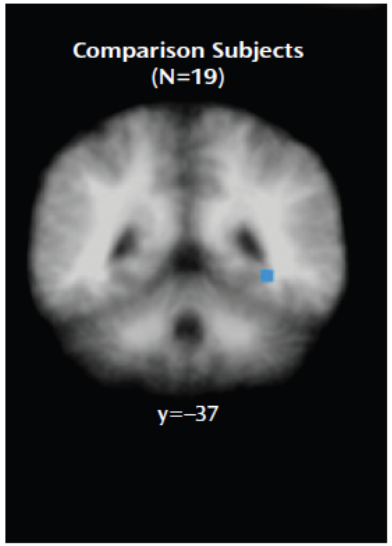
Am J Psychiatry. 2010 Jul;167(7):836-44. Epub 2010 May 3.

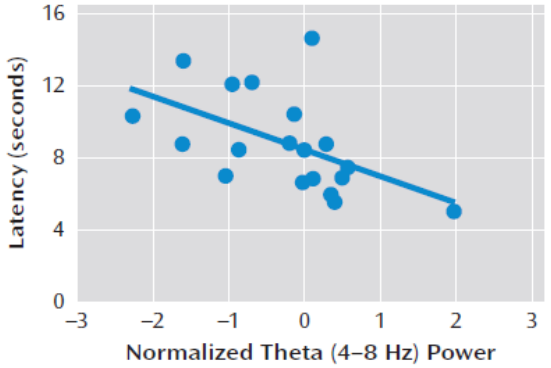
Abnormal hippocampal functioning and impaired spatial navigation in depressed individuals: evidence from whole-head magnetoencephalography.

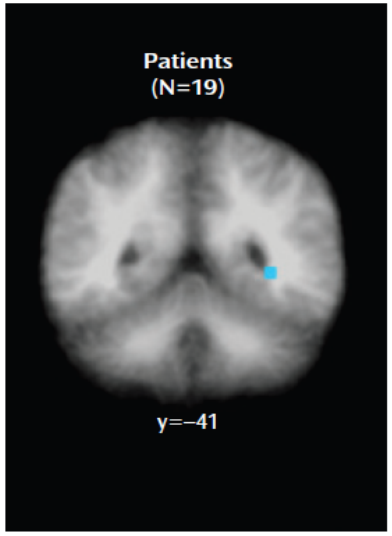
Cornwell BR, Salvadore G, Colon-Rosario V, Latov DR, Holroyd T, Carver FW, Coppola R, Manji HK, Zarate CA Jr, Grillon C.

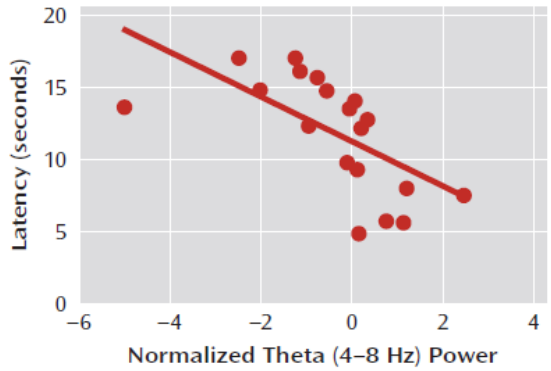
Mood and Anxiety Disorders Program, NIMH, 15K North Dr., MSC 2670, Bethesda, MD 20892, USA.
cornwellb@mail.nih.gov

Hippocampal activity during navigation correlates with time-to-target

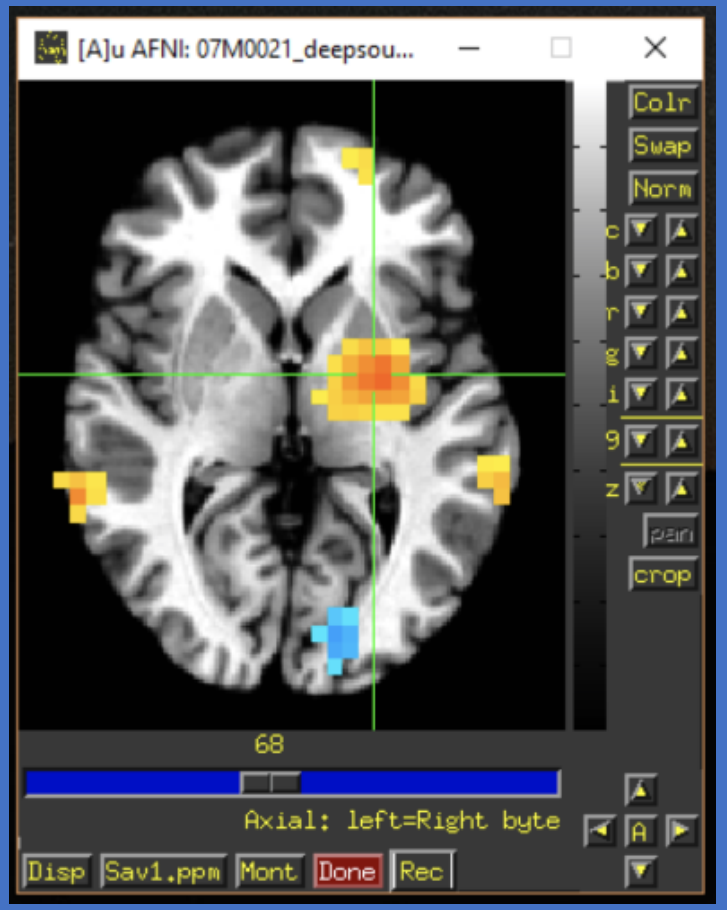


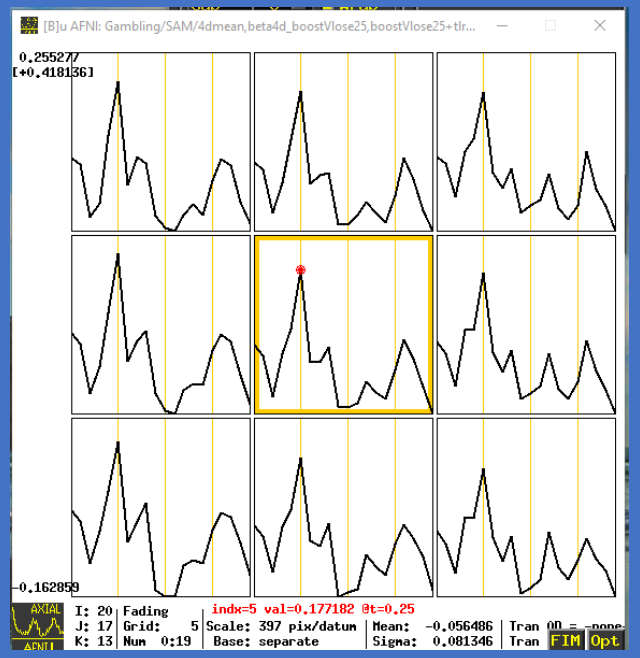






Basal Ganglia

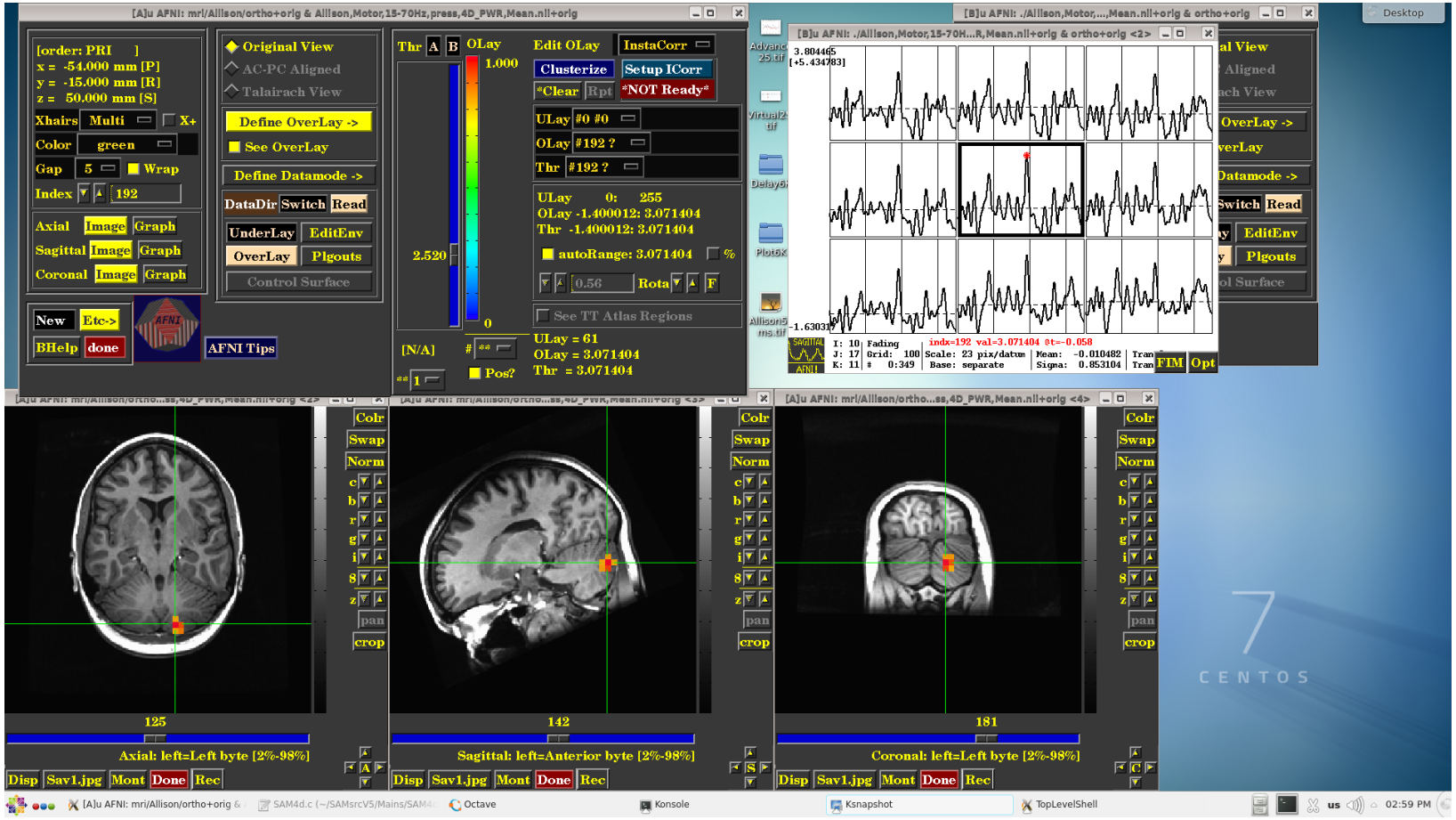




Left Putamen during reward processing

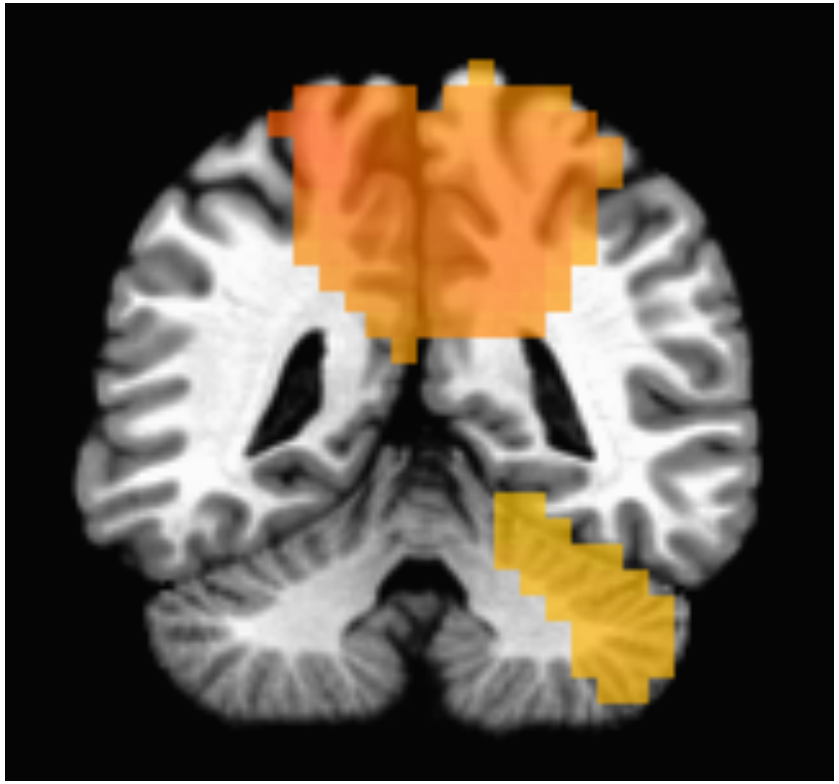
Research by
Linnea Sepe-Forrest
IRTA MEG Core

Cerebellum



Finger tapping by Allison Nugent; Recording by Tom Holroyd; Analysis by Stephen Robinson

Cerebellum + bilateral midline + high gamma

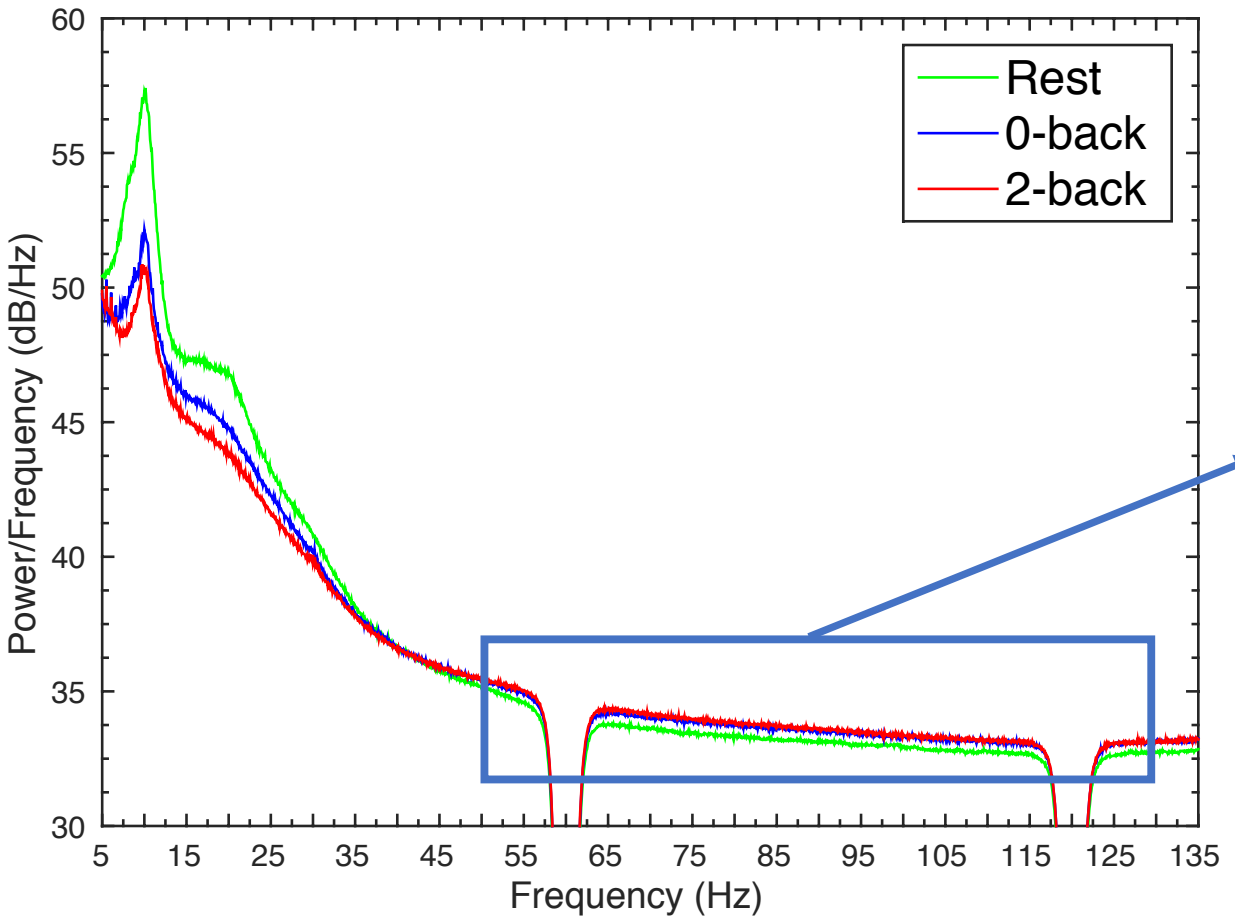


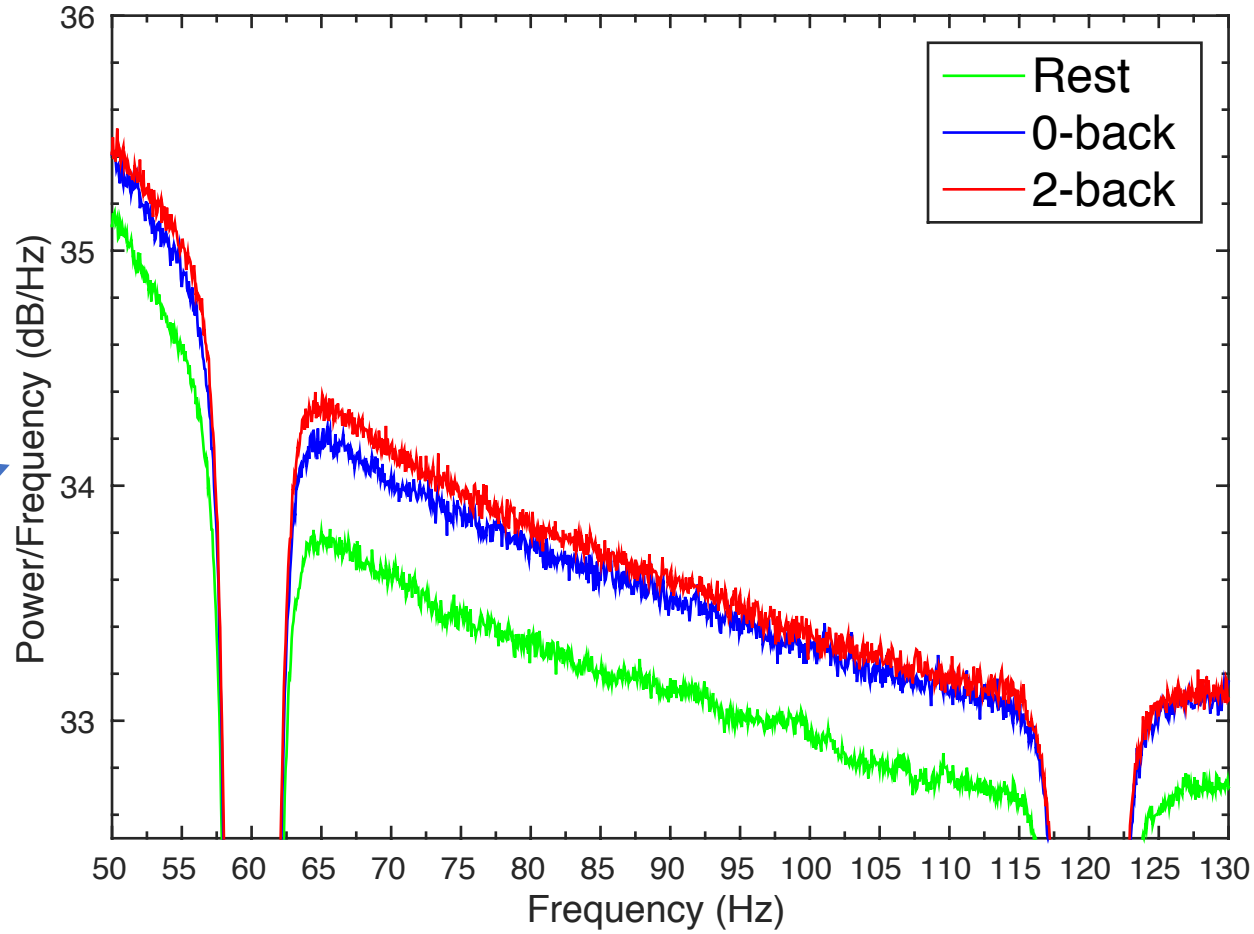
Visuomotor Coordination

High Gamma (65-115Hz) during a joystick center-out reaching task

High Gamma – Spiking?

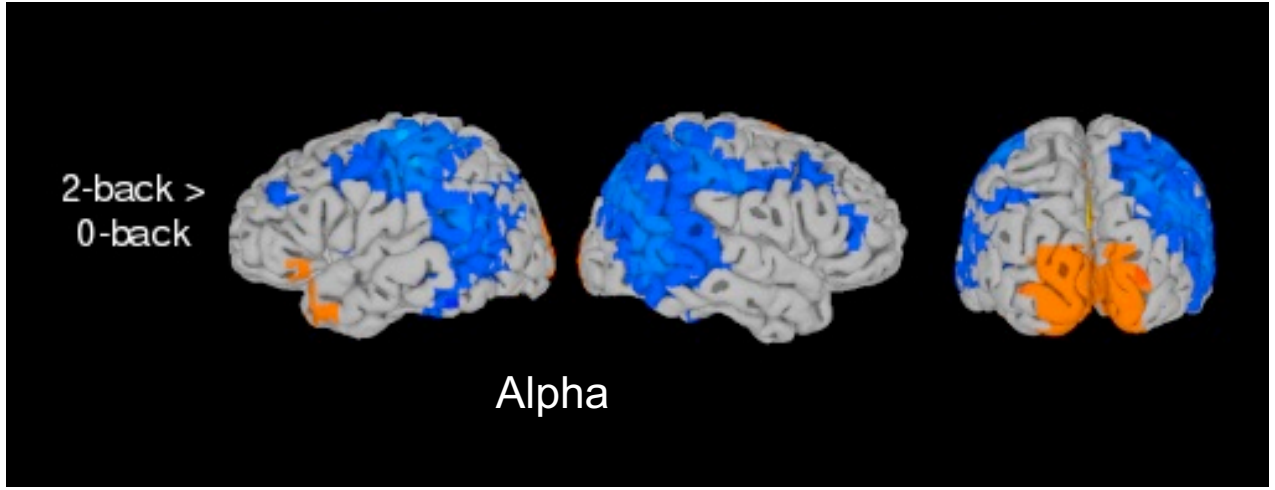
Carver et al. 2019





N-back Working Memory Task compared to Rest

Broad Flat High Gamma similar to Spiking in ECoG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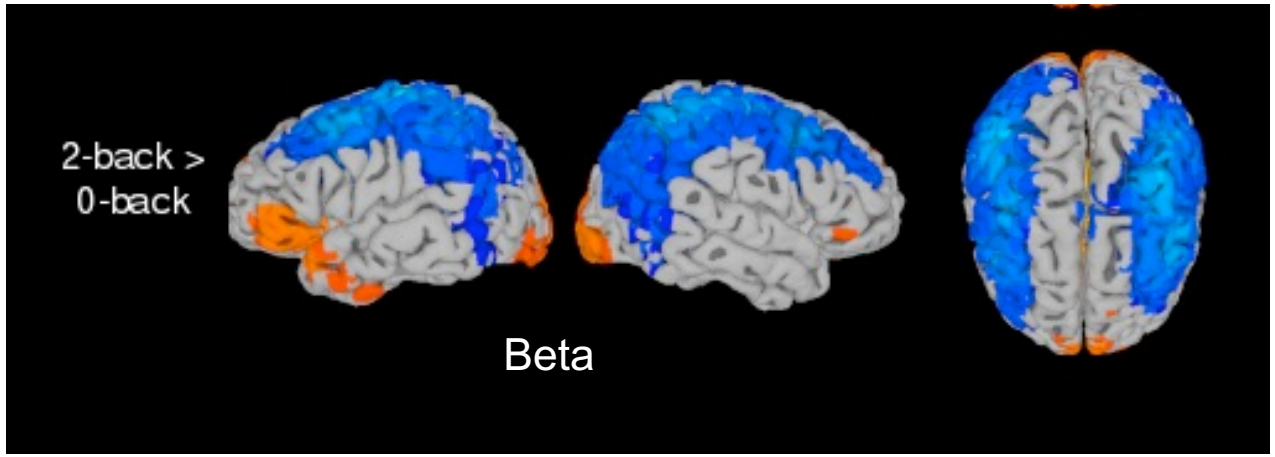
0-back
Alpha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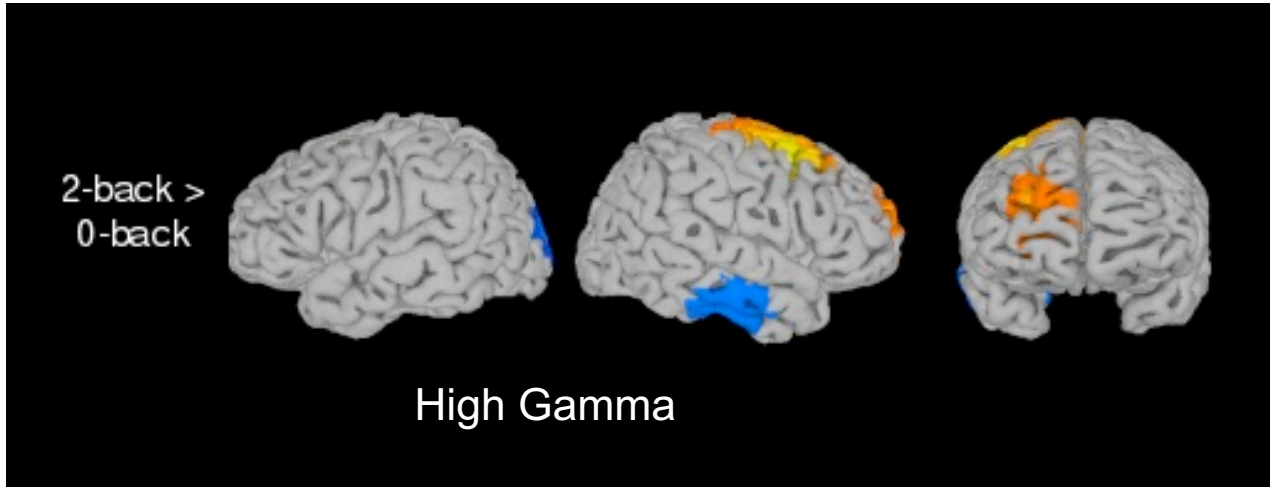
Beta


2-back >
0-back
High Gamma

Summary

- What have we learned?
- Theory doesn't always match reality.
- MEG has improved, both technology and methods,
- Meaning what used to be 'true' is no longer so,
- But beliefs are sticky,
- We tend to prefer black and whites, apples and oranges, EEG vs. MEG, tangential vs. radial, cortical vs. sub-cortical, ‘can’t’ over ‘kinda hard’.
- Deep sources and other things that don’t fit theory are indeed difficult to see, but we are making progress.

Thanks!

- MEG Core Staff
  - Allison Nugent, Director
  - Tom Holroyd, Staff Scientist
  - Stephen Robinson, Staff Scientist
  - Anna Namyst, Lab Manager
  - Linnea Sepe-Forrest, IRTA
  - Katie Shrout, Summer Intern
- Website: megcore.nih.gov, my email: carverf@nih.gov
- Email us to join our mailing list and/or slack page
- Journal club once a month