Other Applications for Speech and Language Processes

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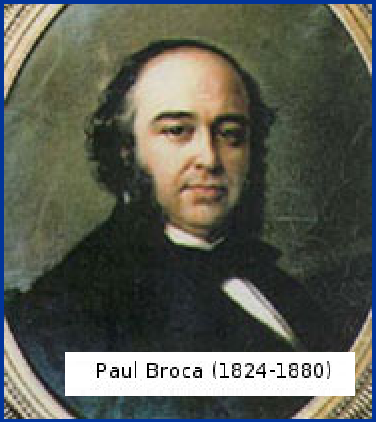
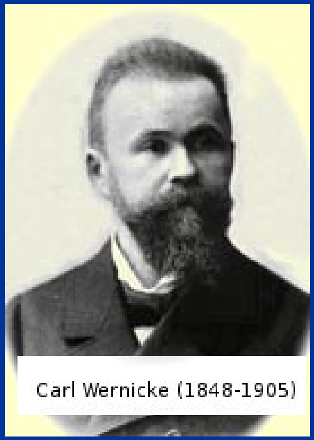
www.megimaging.com

Understanding How Our Brain's Process Language



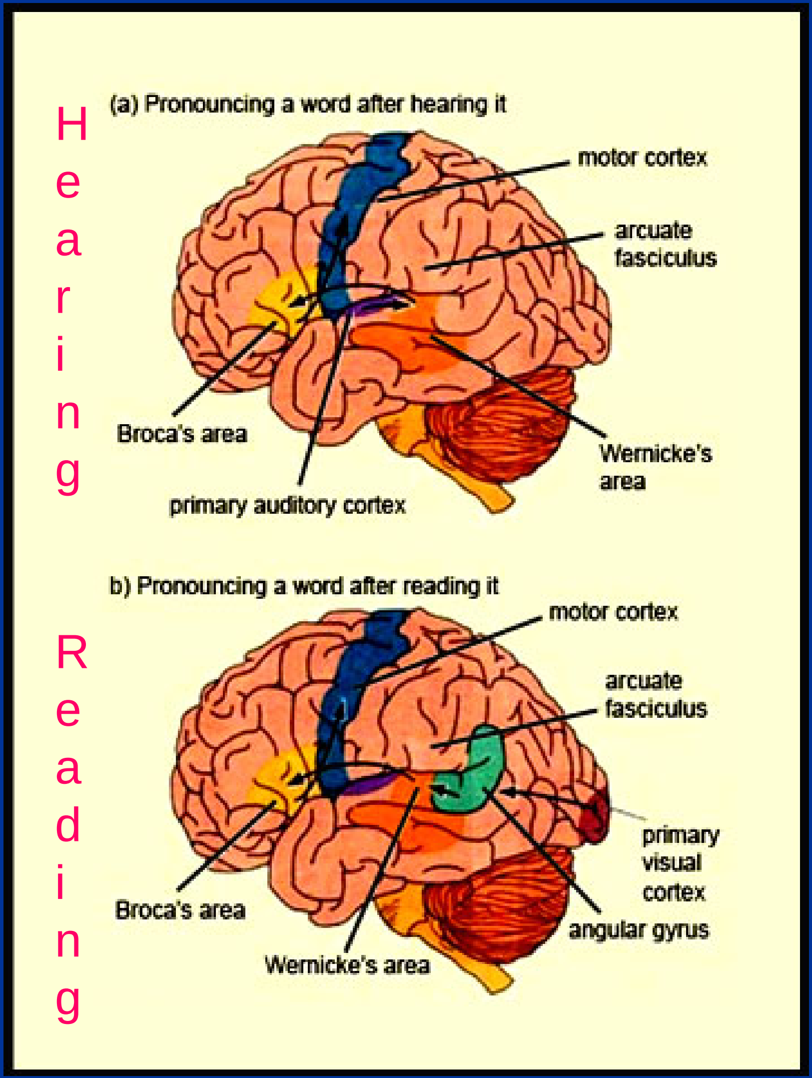
Paul Broca (1824-1880)



Carl Wernicke (1848-1905)

1861 Broca, a French neurosurgeon, found a lesion in the Left inferior frontal cortex of a man who could not speak.

Ten years later, Wernicke, a German neurologist, discovered people who had a lesion in the left temporal lobe could speak, but their speech was often incoherent and made no sense.



Website: The Brain from Top to Bottom

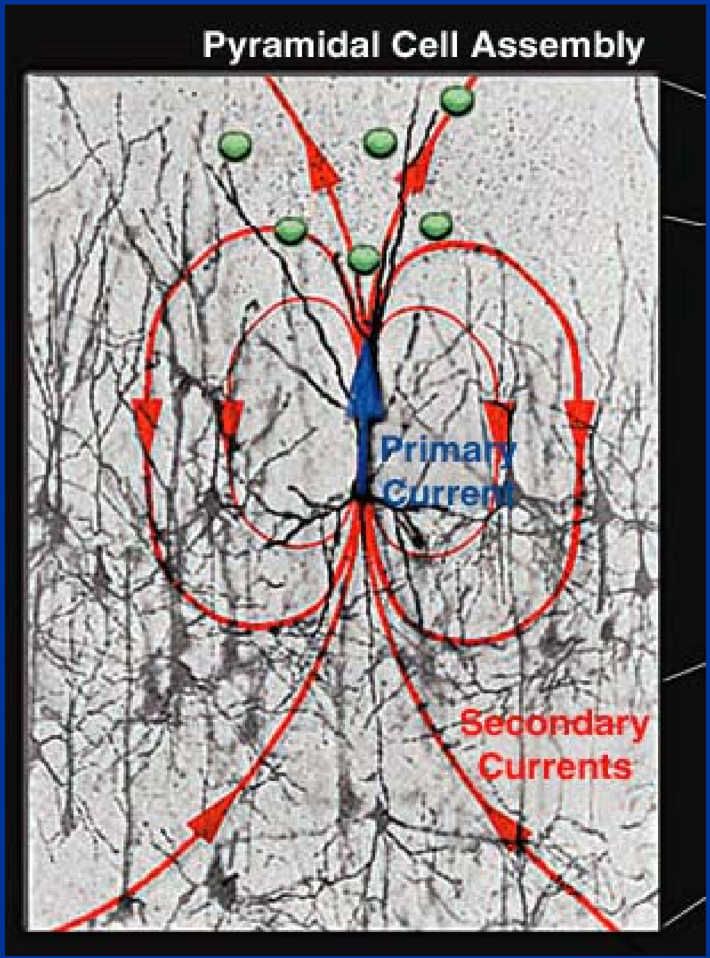
Sources of the signals

Neuronal

- MEG signals primarily arise from intracellular current flow in pyramidal neurons (Primary Currents)
  - EPSPs and IPSPs
- EEG signals primarily arise from extracellular current flows (Secondary Currents)
  - Volume currents

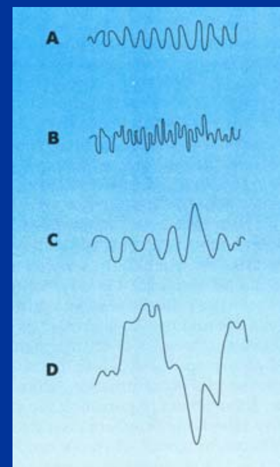
Metabolic

- fMRI signals arise from an increase in blood flow to the local vasculature when neural activity occurs. This results in a corresponding local reduction in deoxyhemoglobin because the increase in blood flow occurs without an increase of similar magnitude in oxygen extraction.
- PET signals arise from an increase in glucose (Fludeoxyglucose or the tracer) consumption that accompanies neural activity. The system detects photon emissions from a positron-emitting radionuclide (tracer)



Functional Imaging Techniques
Great Temporal Resolution

Electroencephalography EEG



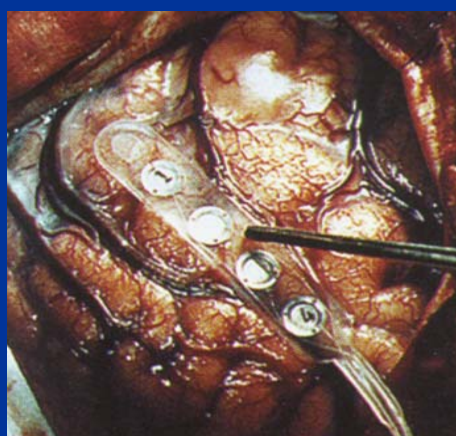
Alpha (8-12 Hz)

Beta (13-30 Hz)

Theta (4 - 8 Hz)

Delta (< 4 Hz)

Gamma (> 30 Hz)



Electrocorticography ECoG

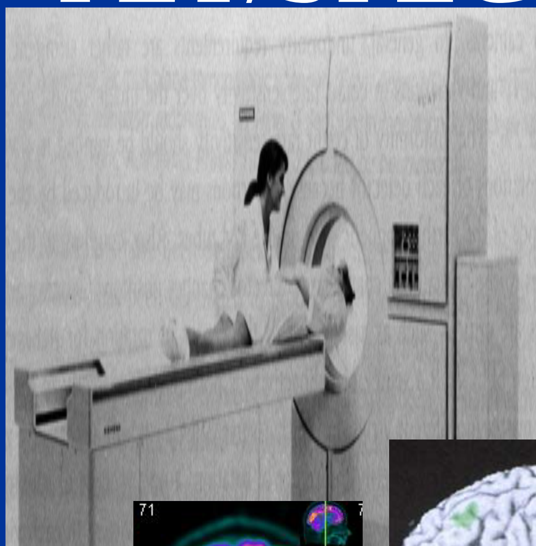
"THE GOLD STANDARD??"

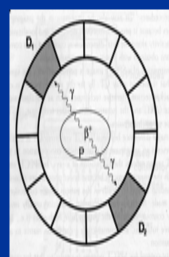
Magnetoencephalography MEG

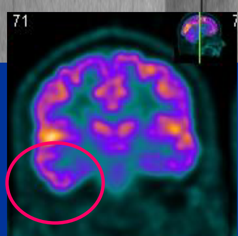
Functional Imaging Techniques
Great Spatial Resolution

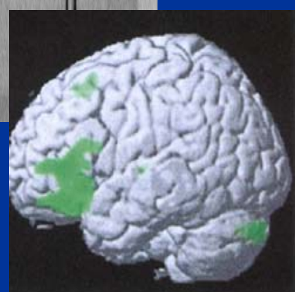
Positron-Emission Tomography

PET/SPECT





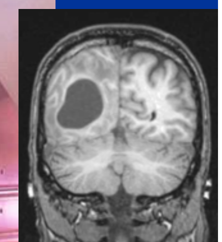




Functional Magnetic Resonance Imaging

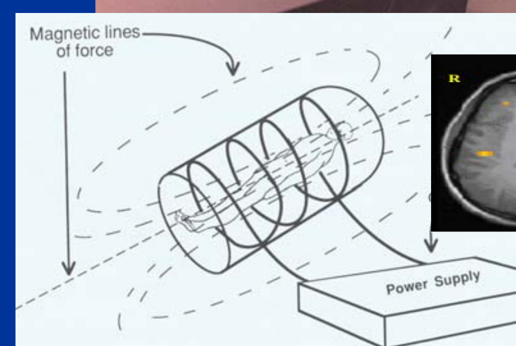
fMRI

A technique for measuring blood oxygenation of specific tissue during a task.



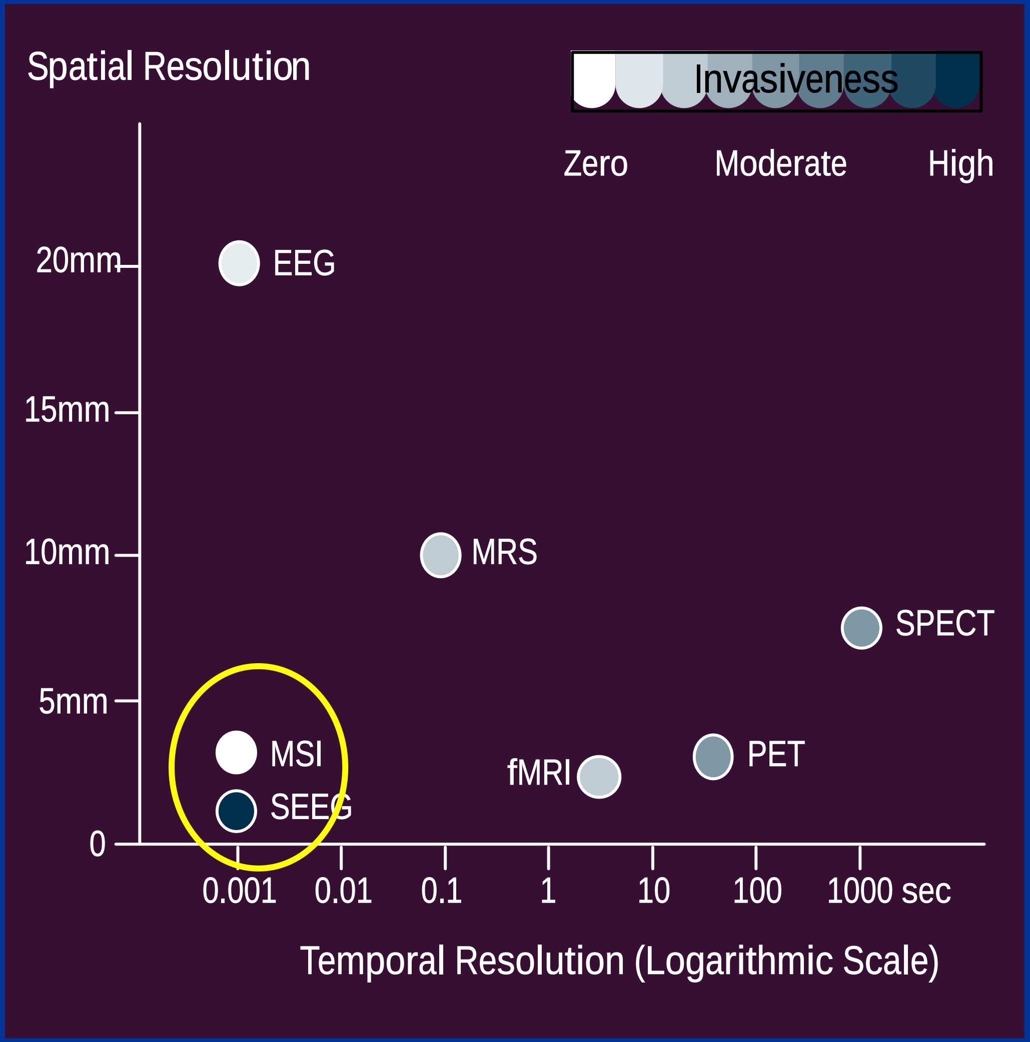
Both techniques overlay Pixel activation onto an MRI scan

Directly images metabolism



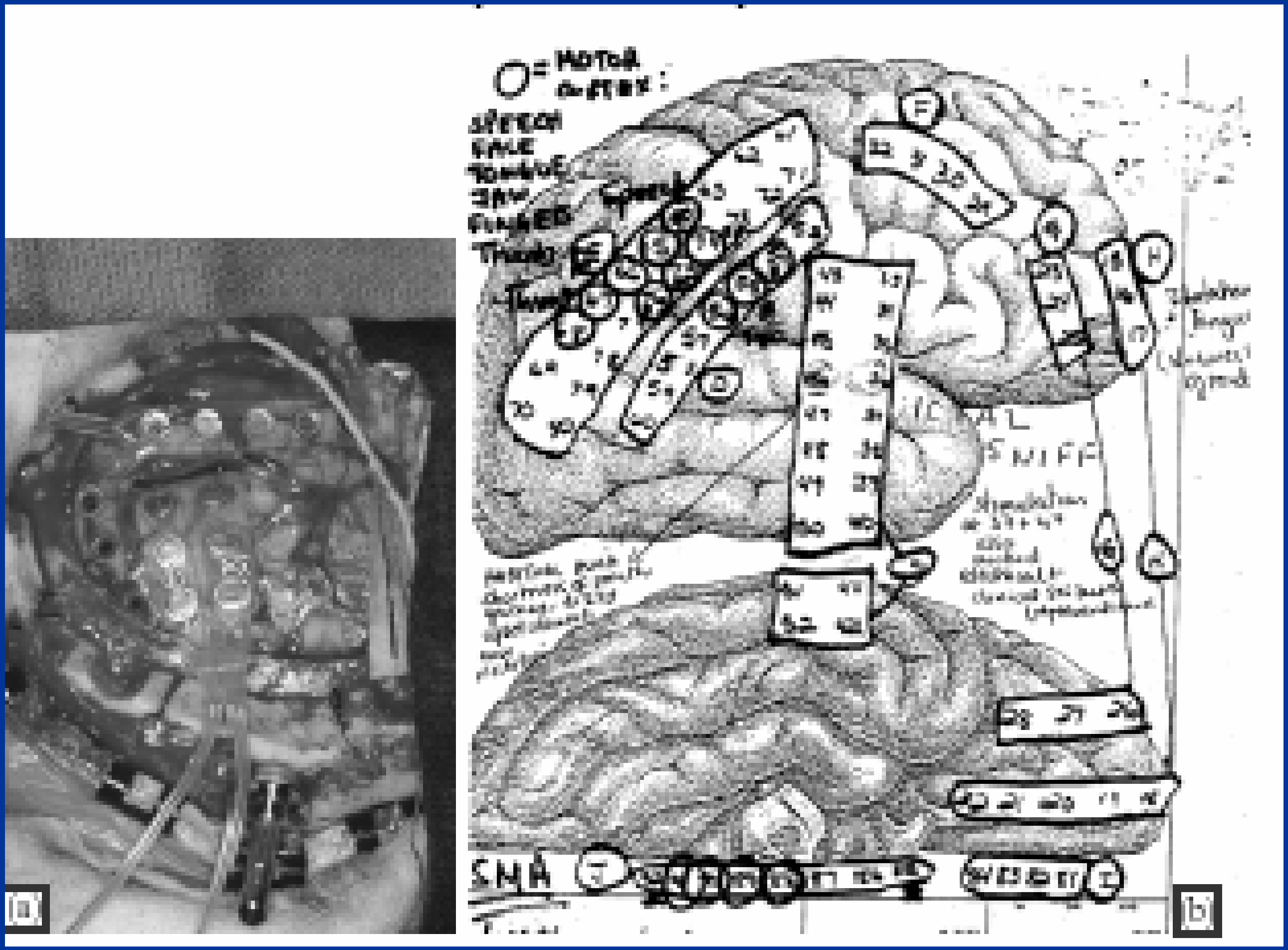
A technique for studying the metabolism of the brain, by using positron-emitting isotopes ^{11}C, ^{13}N, ^{15}O, and ^{18}F labeled molecules in solution and injected into a subject.

Spatial and Temporal Resolutions for Various Functional Imaging Modalities



4D Neuroimaging

Electrocorticography Localization



Subdural electrodes placed on cortical surface.
Typical 2D views of the brain diagram used to mark the electrode locations and hand written schematic results of the brain mapping tests.

Language locations by ECoG

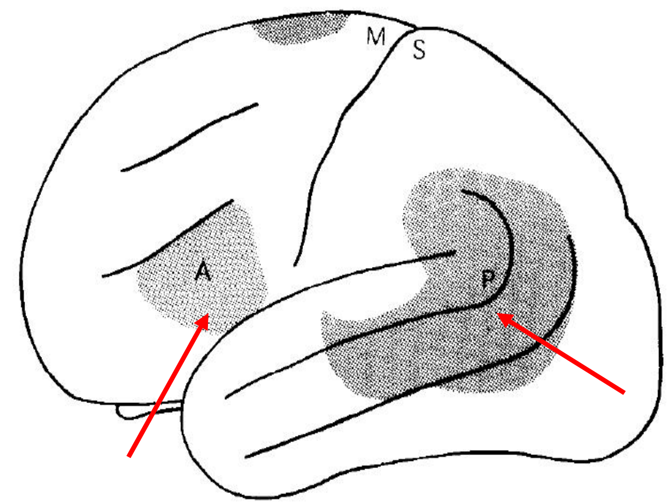


Figure 2. Location of essential cortical areas for language in the traditional textbook model, here as presented in Penfield and Roberts (1959), are indicated by shading. *A*, frontal (Broca's) language area; *P*, posterior (Wernicke's language area); *M* and *S*, motor and sensory cortex. Compare to language localization in an individual subject (Fig. 1) and variance in that localization across a population (Fig. 3).

Penfield and Roberts 1959

Essential sites for naming

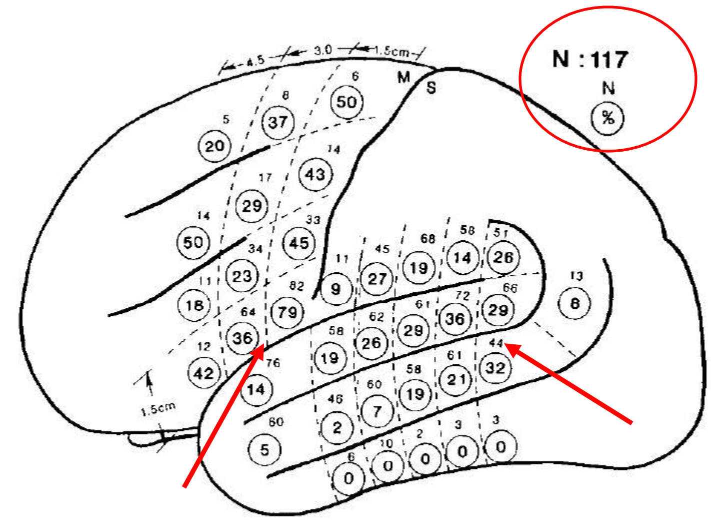
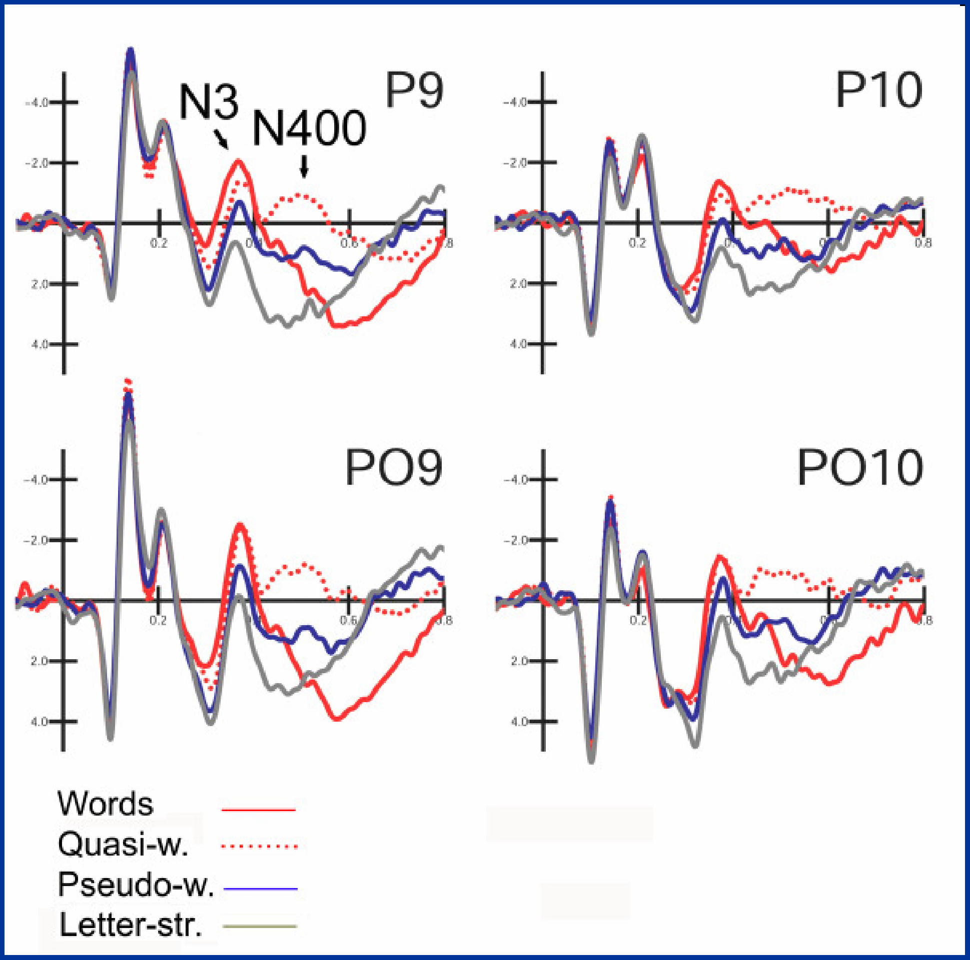


Figure 3. Variability in localization of sites essential for naming, based on electrical stimulation mapping in left, language-dominant hemisphere of 117 patients. Individual maps, such as Figure 1, were aligned with reference to Rolandic cortex and end of Sylvian fissure. The cortex was then divided into zones represented by intersecting *solid* and *broken lines*. The *upper number* in each zone indicates the number of subjects in whom a site was tested in that zone; the *lower circled number* indicates the percentage of those subjects in whom naming errors were evoked at sites in that zone. *M* and *S* indicate motor and sensory cortex, respectively. From G. Ojemann et al. (1989).

Ojemann et al 1989

Errors in current spreading on cortex

EEG Results



Proverbio and Adorni Behavioral and Brain Functions 2008

Combined fMRI and PET

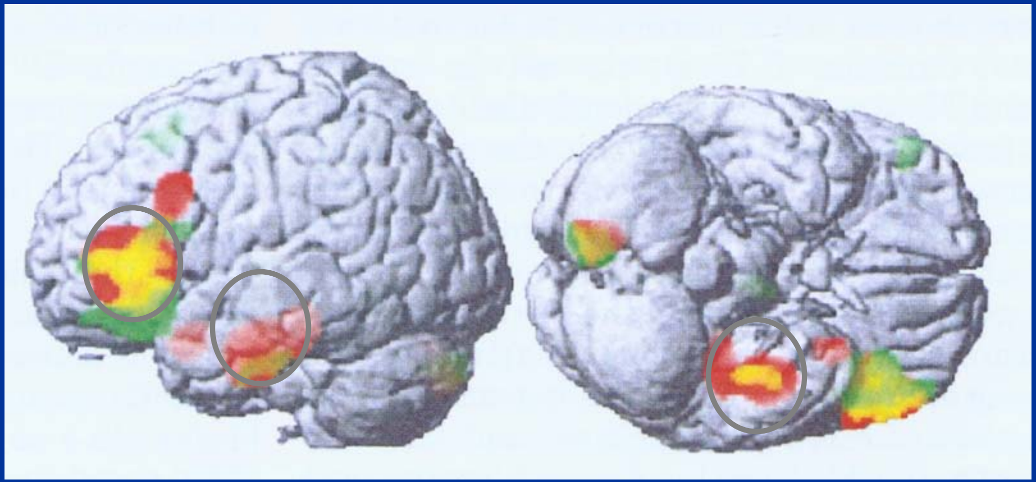
fMRI

PET

Semantic minus Letter categorization comparison task

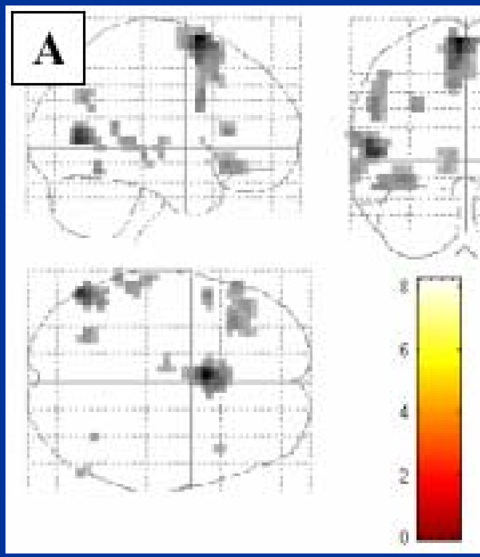
Yellow color is where fMRI and PET results overlap

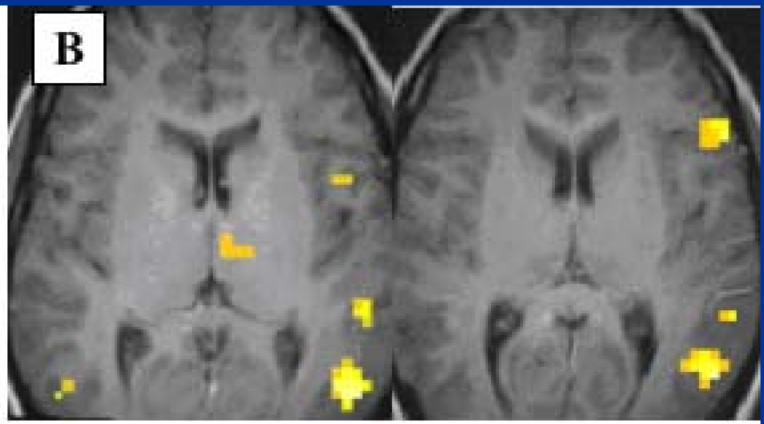
Task :
Subjects read three cue words presented one after another and then made a decision about whether a fourth (target) word belonged to the same category as the cue words



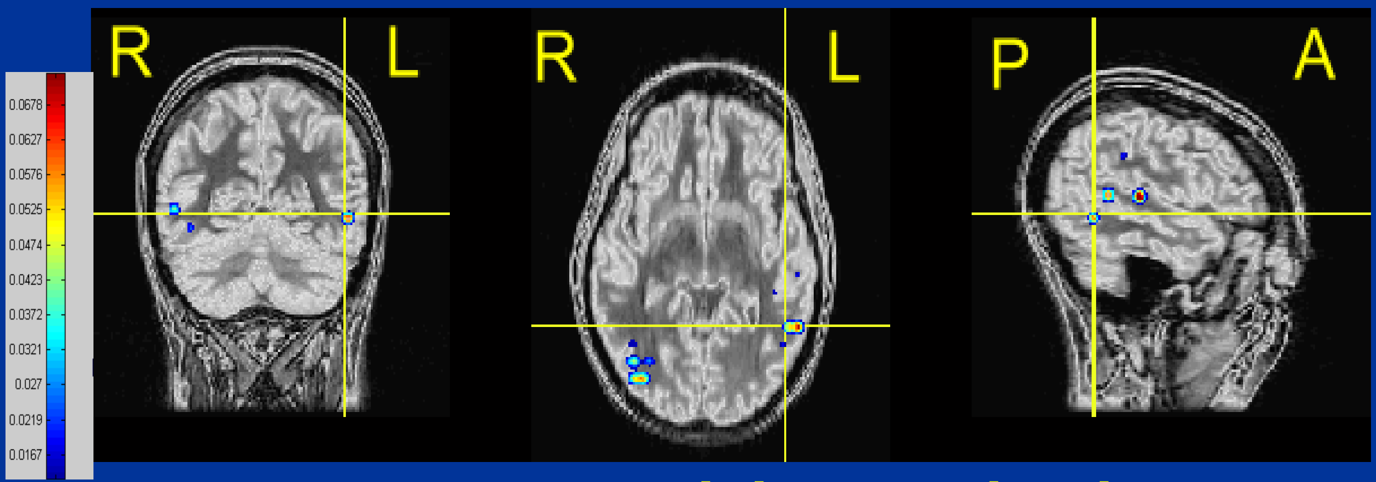
Devlin et al, NeuroImage 11:589-600, 2000

fMRI and MEG during Verb Generation





fMRI localization of brain areas active during verb generation. SPM maps. A) Three-plane Glass Brain (Fixed effect analysis corrected p<.001) B) Axial overlay shown. Z-score scale shown in color bar.



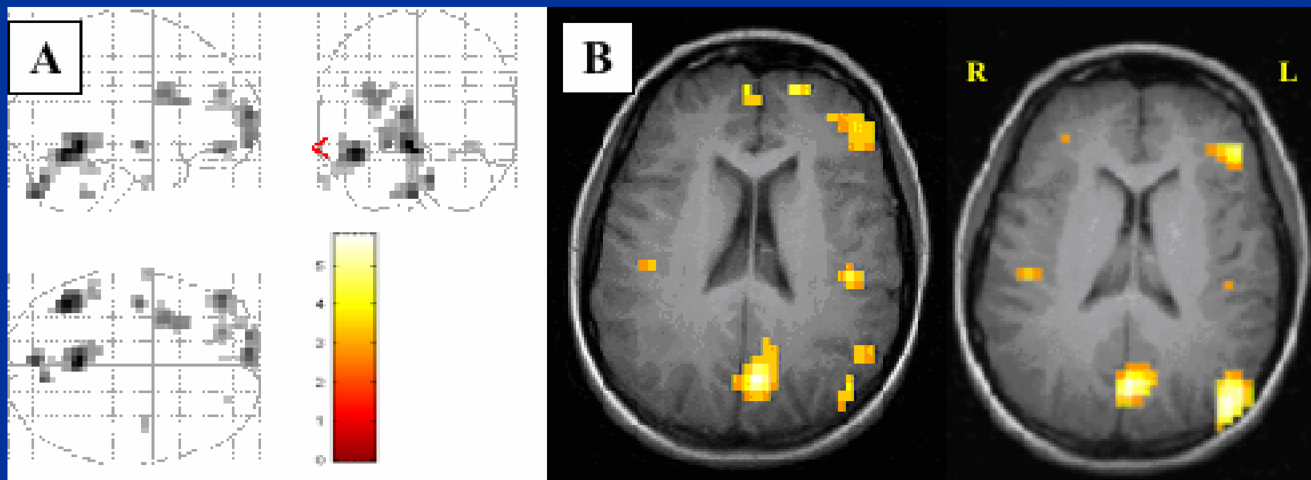
nanoAmp-meters

MEG localization at 255 ms after onset of Visual word. This is the point at which the brain is generating the verb. MR-FOCUSS results scale in nanoAmp-Meters

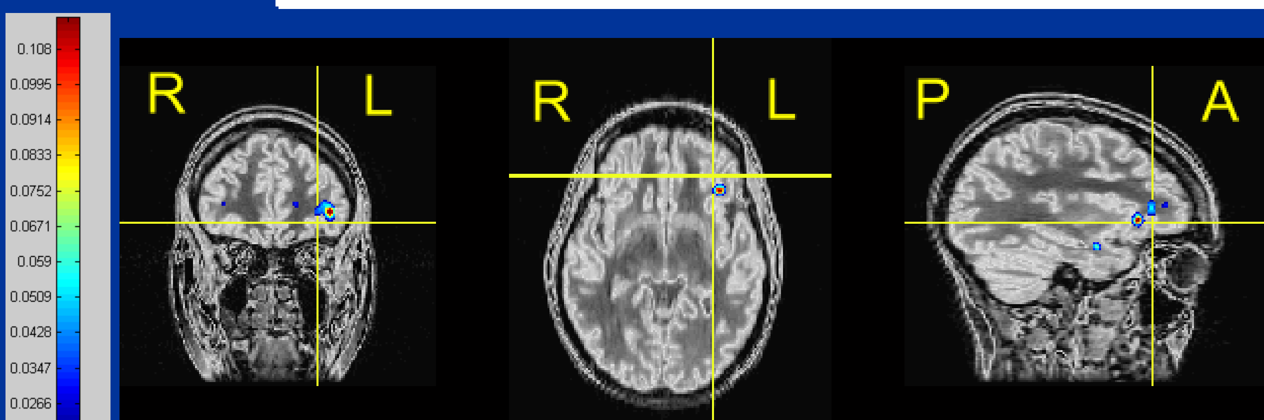
Wernicke’s activation

Bowyer et al, Neurology, 2004

fMRI and MEG during Picture Naming



fMRI localization of brain areas active during Picture Naming. SPM maps. A) Three-plane Glass Brain (Fixed effect analysis corrected p<.001) B) Axial overlay shown. Z-score scale shown.



nanoAmp-meters

MEG localization at 320 ms after onset of Visual picture. This is the point at which the brain is telling the mouth to say the word. MR-FOCUSS results scale in nanoAmp-Meters

Broca's activation

Bowyer et al, Neurology 2004

Language Guidelines

INVITED ARTICLE

American Clinical Magnetoencephalography Society Clinical Practice Guideline 2: Presurgical Functional Brain Mapping Using Magnetic Evoked Fields*

*Richard C. Burgess,† Michael E. Funke,‡ Susan M. Bowyer,§ Jeffrey D. Lewine,‖ Heidi E. Kirsch,¶ and Anto I. Bagić,#; for the ACMEGS Clinical Practice Guideline (CPG) Committee**,****

(*J Clin Neurophysiol* 2011;28: 355–361)

Like other laboratory tests, it is important that clinicians

Guidelines for Language

Indications

- Determining the language-dominant hemisphere in patients with either organic or functional brain diseases before surgical interventions, such as craniotomy, stereotactic or radiosurgical procedures; and/or
- Objective functional evaluation of language processing (i.e., identification of location and latencies).

Journal of Clinical Neurophysiology • Volume 28, Number 4, August 2011

Recording (Data Acquisition)

- Band pass of 0.03 to 300 Hz with a digitization rate of 1,000 Hz is preferred to facilitate postprocessing of the raw data.
- MEG recording for language should be continuous.
- Triggers must be simultaneously recorded for segmenting data and averaging the evoked waveforms in postprocessing analysis.
- The data processing is similar to that used for all evoked responses.
- Online averaging runs the risk of including trials with large movement artifacts and/or eye blinks and should generally be avoided, or employed in real-time only to assess proper system operation.
- Head position measurement should be carried out before each ensemble or data block. Use of continuous head position tracking is preferred if available.
- Performance of the same task should be replicated during the same session. Independent analysis of the two data sets can help to minimize sources of error (i.e., head movement, changes in performance, attention level, variations in background activity, coregistration errors).

Data Analysis

Averaging

- When magnetic signals are small, continuously recorded data can be averaged off-line to improve the SNR.
- Averaging over the multiple time epochs is valid only when intracranial events are assumed to be identical.
- Adequate SNR for LEFs can be typically achieved with 50 to 100 artifact-free trials.
- Early evoked fields can be used for quality control (latency, topography). For example, if stimuli are presented acoustically, the auditory N100m responses should be symmetrical in topography, peaking around 100 milliseconds and with similar amplitude.
- Data should be typically band-pass filtered 1 to 50 Hz.

Initial inspection of data

- Before considering the analysis of long-latency language-related activity, it is important to evaluate the integrity of basic auditory/visual responses at ~100 milliseconds.
- Tumors and other lesions can cause lateralized compromise of basic sensory (auditory/visual) processing if located in primary or secondary sensory (auditory/visual) areas. If core sensory processing (auditory/visual) is compromised, special caution is needed in the interpretation of long-latency activity.
- Raw data used to generate averages should also be inspected. Lateralized paroxysmal spikes, sharp waves, and slow waves can have a dramatic effect on evoked responses and lead to

Hemispheric dominance for language

- The determination of hemispheric dominan based on an assessment of how much la evoked in each hemisphere, as assessed evoked field.
- Several strategies are available for source a ing single and multiple dipole based strat reconstructions such as L1 norm, L2 norm, and beamformers. Different laboratories have used different methods, but the most commonly used methods are based on dipoles and minimum norm estimates.
- One of the most commonly used methods is to use single moving dipoles to account for the activity beyond 150 milliseconds. In this method, at each time point, a restricted sensor array is identified encompassing the long-latency response(s). A single equivalent current dipole is calculated and if the goodness of fit exceeds a prespecified criteria (e.g., 90%), then the fits are considered valid and the dipole is retained. After all time points are fit (typically in 1-millisecond steps), a laterality index is calculated based on the number of valid dipole fits in each hemisphere. Here, laterality index is defined by $100 \times (R - L)/(R + L)$, where L and R are the number of accepted dipoles fit in the left and right hemispheres, respectively. Laterality index values from -100 to -20 indicate strong left hemisphere language dominance. Laterality index values from -19 to $+19$ indicate bilateral language activation. Laterality index values from $+20$ to $+100$ indicate right hemisphere language dominance.

Language organization and reorganization in epilepsy

- Most healthy individuals are left hemisphere dominant for language
- Patients with Epilepsy in the left hemisphere epilepsy have a higher likelihood of atypical language organization
- The cerebral organization of language in epilepsy has been studied to explore the influence of unique clinical features inherent in epilepsy that might contribute to the reorganization of language, such as location of seizure onset, age of seizure onset, and extent of interictal epileptiform activity.
- Unlike the abrupt language changes that occur following acute brain injury with disruption of established language circuits, converging evidence suggests that the chronic nature of epileptic activity can result in a developmental shift of language from the left to the right hemisphere or re-routing of language pathways from traditional to non-traditional areas within the dominant left hemisphere.
- The use of imaging techniques are needed to reliably predict altered language networks in individual patients to provide definitive identification of language cortex for lateralization and localization necessary for clinical care.

Hamberger &, Cole Neuropsychol Rev. 2011

Alternative methods for Analyzing MEG Language Recordings

- A common alternative method is to use a distributed source model (e.g., MR-FOCUSS) and compare the integrated amount of current in left and right hemispheres over the LEF time window. This can be done across all activated regions, or specified regions (e.g., basal temporal areas). Here too, it is common to derive a laterality index, based on source signal strength as opposed to number of dipole fits.
- Alternative analyses, including beamforming strategies and multiple dipole strategies, may also be viable. The key is to integrate information over the long-latency time window and to examine data within the context of a source model that accounts for the subject's physical position relative to the sensors.

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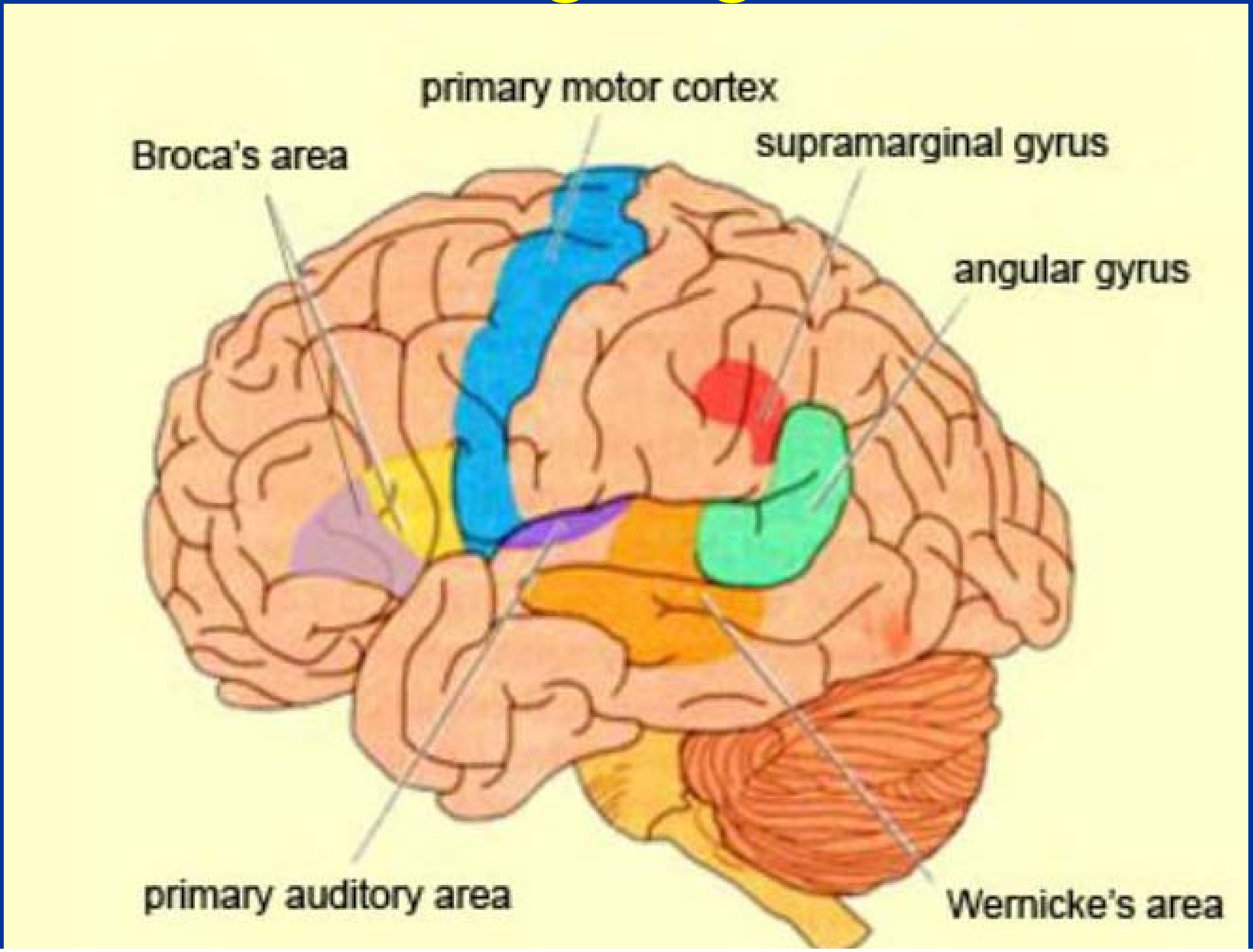
OTHER MEG techniques!

In 2008 - 15 of the 21 USA MEG centers Practiced Clinical MEG
all used ECD analysis techniques

- Current Density or Distribution
  - Milliseconds
- Beamforming
  - 24-50 millisecond averages
- Coherence Imaged (not in Sensor space)
  - Collapses time

Bagic, J Clinical Neurophy 2011

Language Areas



Language has both localized and distributed patterns of brain activity

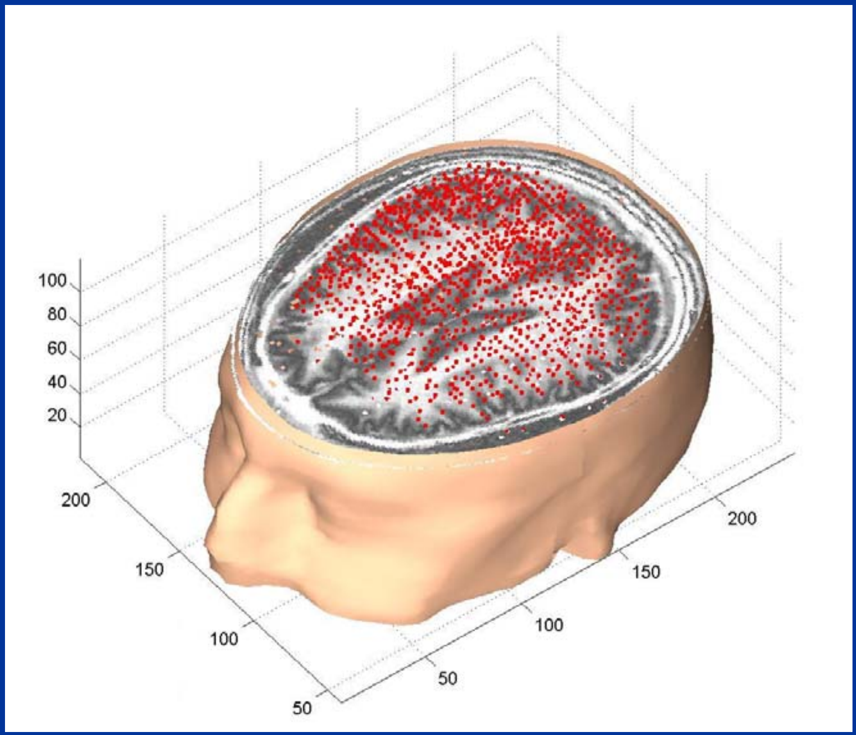
Website: The Brain from Top to Bottom

MR-FOCUSS/Minimum Norm

- A non-linear current density imaging technique
- Images extended and compact sources of neuronal activity.
- Incorporate a wavelet basis to obtain a multi-resolution description of the cortical source structure
- Performs focal changes of the source structure amplitudes for enhanced imaging of multiple simultaneously active compact sources
- For statistical robustness, ~20 solutions averaged to create images
- Relatively insensitive to noise
- Useful for studying the sequence of interhemispheric neuronal activity
- Can study time evolution of sources
- Available at: http://www.megimaging.com CTF import is available and Neuromag import is coming SOON!

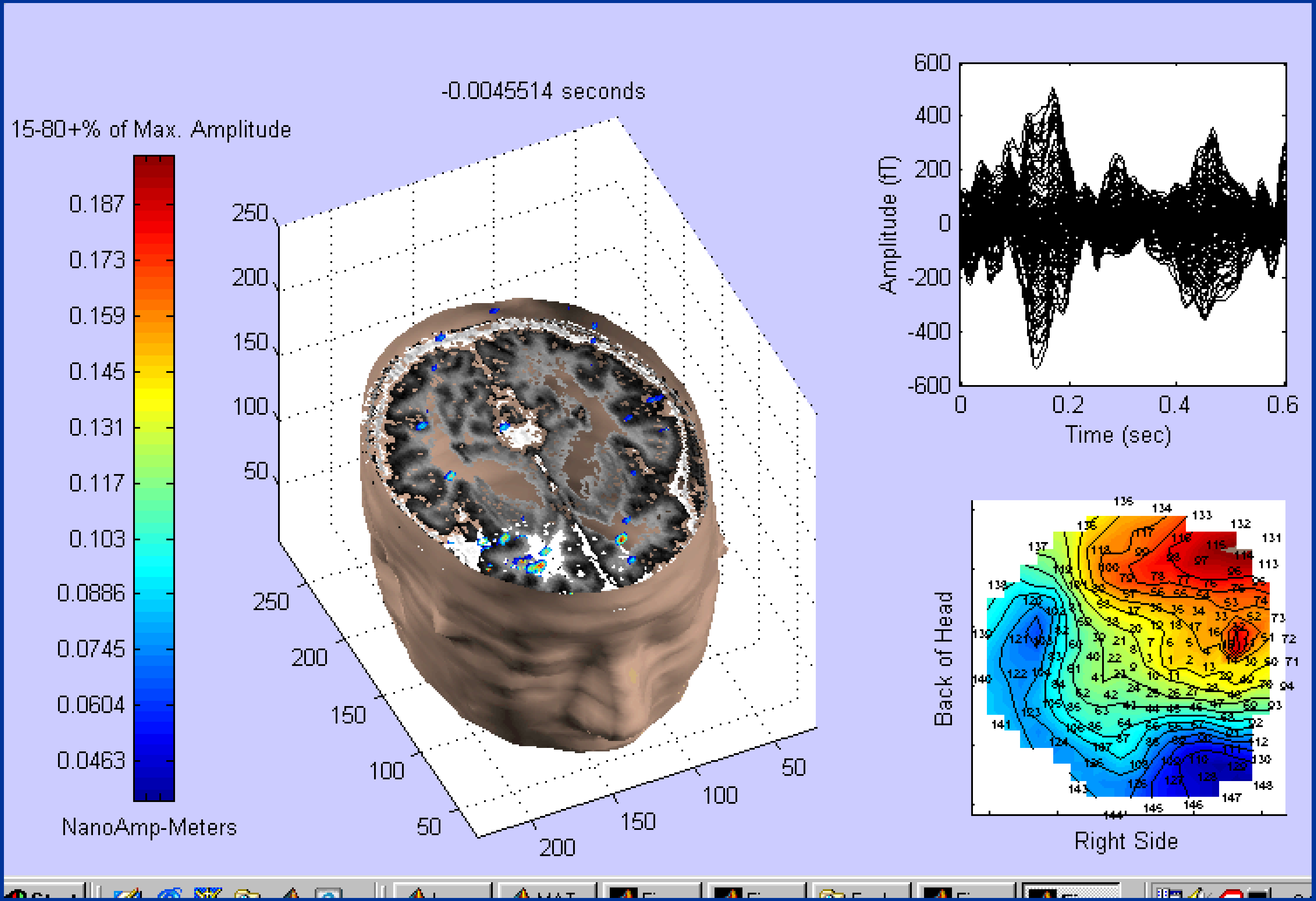
Moran et al, Brain Topography 2005

Cortical Model



- Created from Volumetric MRI Data
- ~4000 cortical locations
- Distribution matches cortical gray matter

Time Evolution of Language Processing



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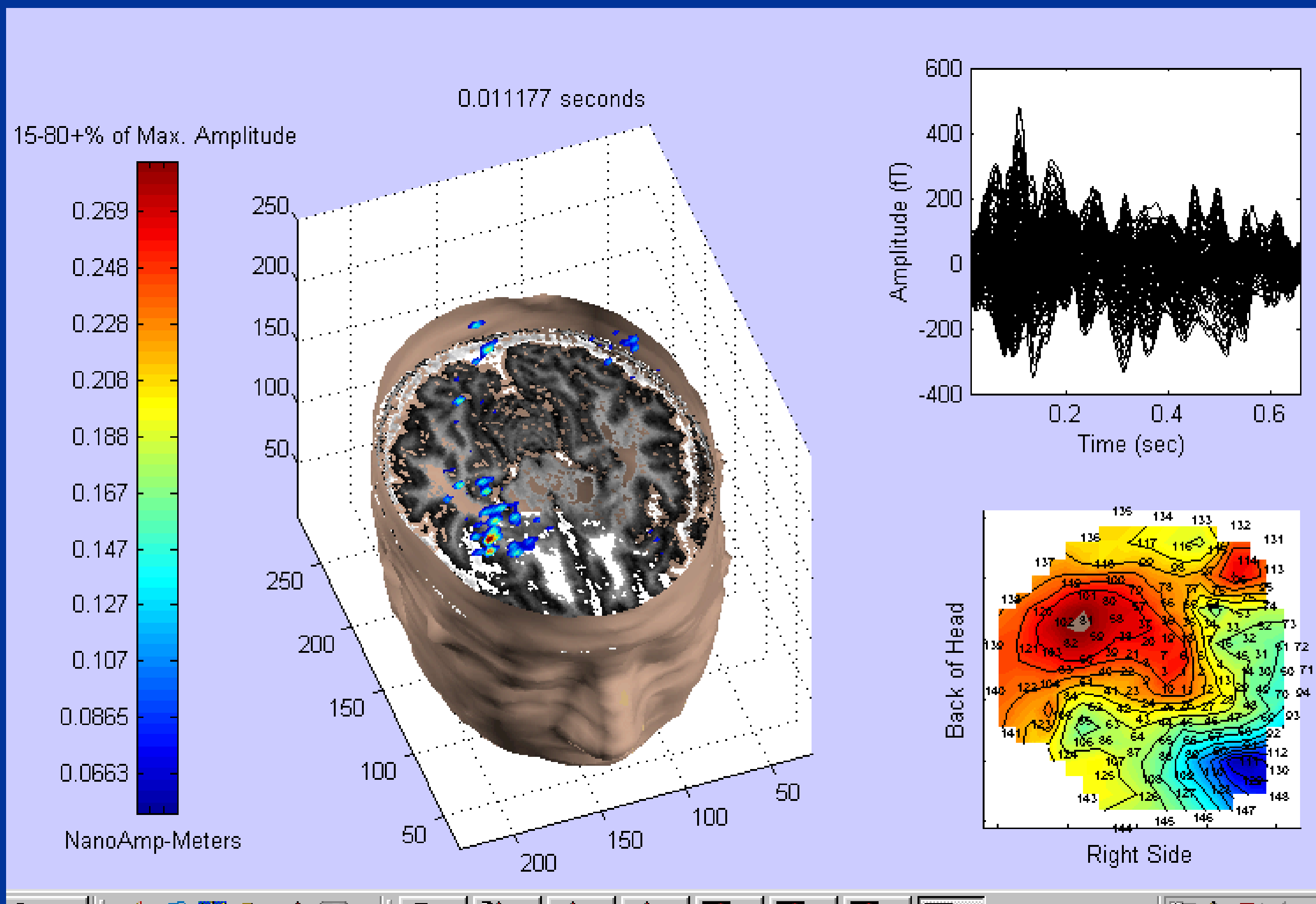
Applications for Dyslexia

Subject with Dyslexia: Picture Naming

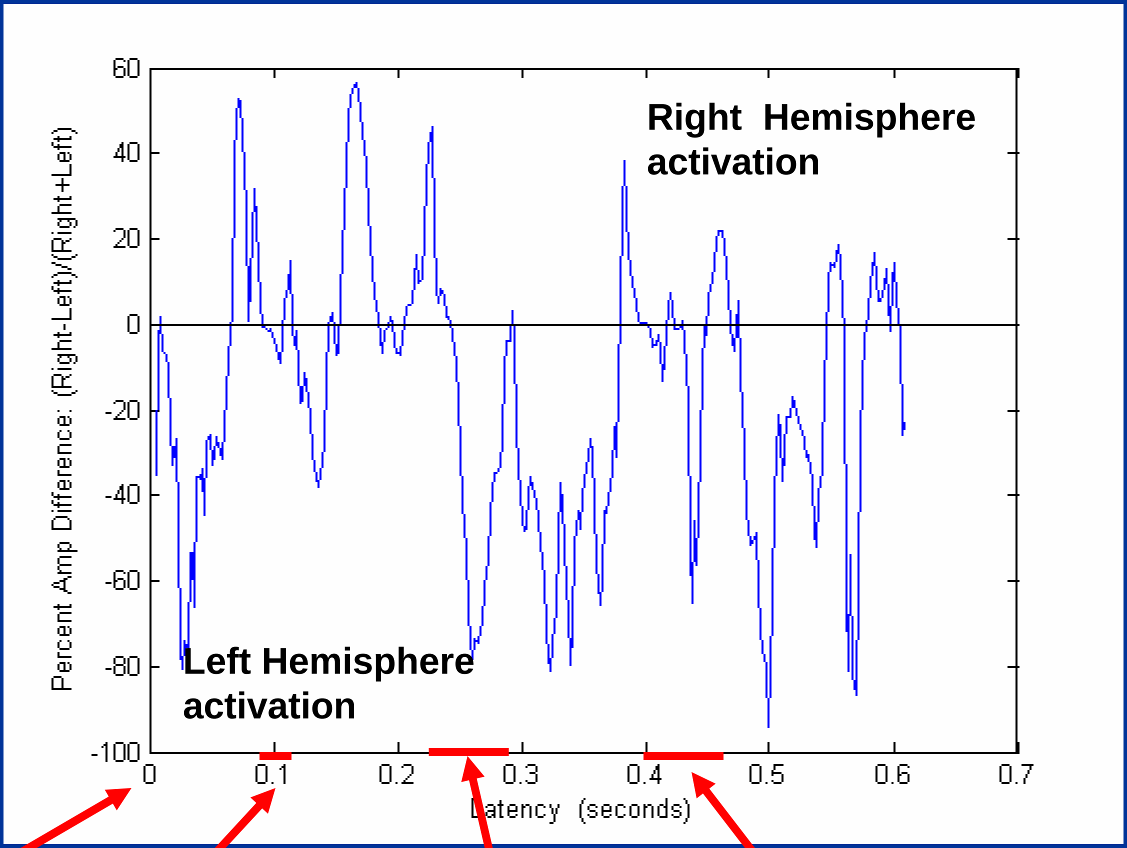


Language Laterality

Picture naming task, brain activity between 396-460ms found closest concurrence with the WADA results (IAP).

In 23 out of 24 epilepsy patients with a successful IAP, the Index for Broca's activation were in agreement with the results of the WADA (96% accuracy).

In 1 of the 3 patients who had an undetermined or bilateral IAP, MEG lateralized language to the same hemisphere as clinical findings making our overall accuracy 89%.



Stimuli onset

Visual processing

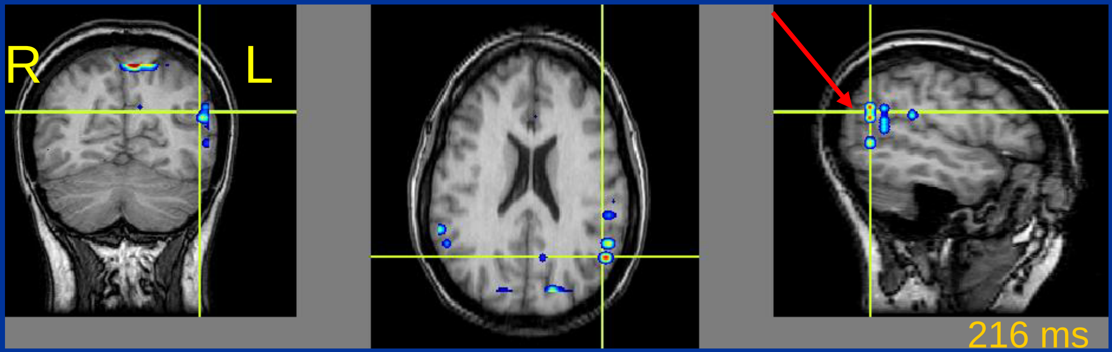
Comprehension (Wernick's) 230-290 ms

Motor speech (Broca's) 396-460ms

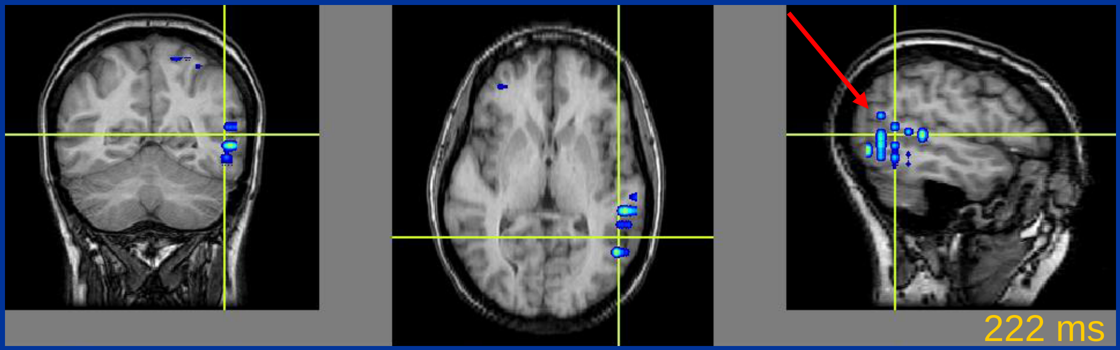
Bowyer et al 2005 Epilepsy & Behavior

MEG Current Distribution for Detecting Dyslexia with Real & Nonsense Word Reading

A. Real word



B. Nonsense word

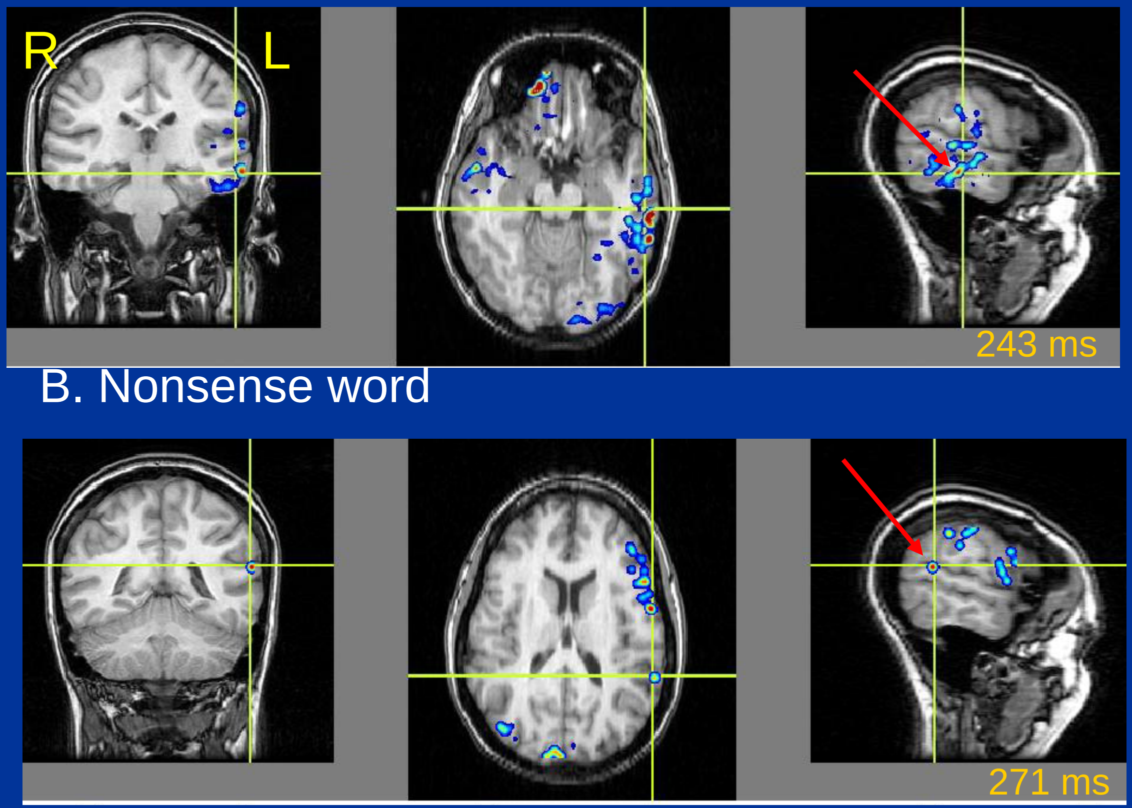


MR-FOCUSS imaging in a right handed, 46 year old normal reader. Angular gyrus on the left side is active in both tasks.

Henry Ford Hospital

Reader with Dysphonetic Dyslexia

A. Real word



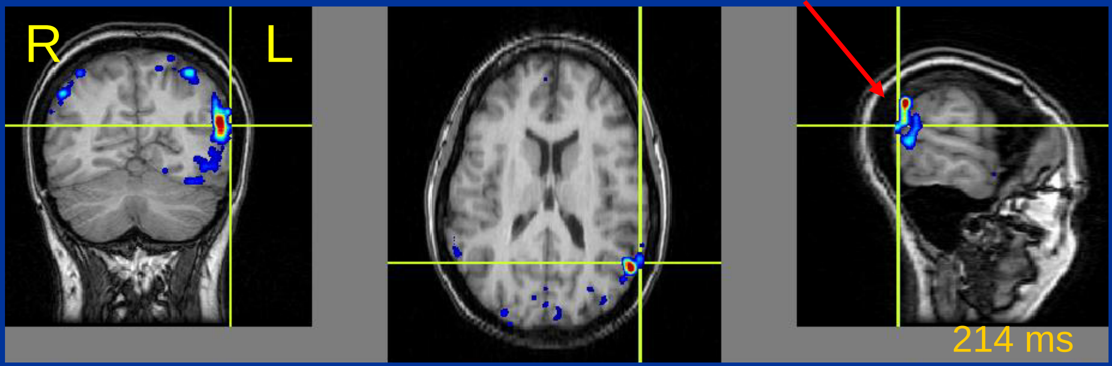
B. Nonsense word

Dysphonetic subjects have problems with putting phonemes together

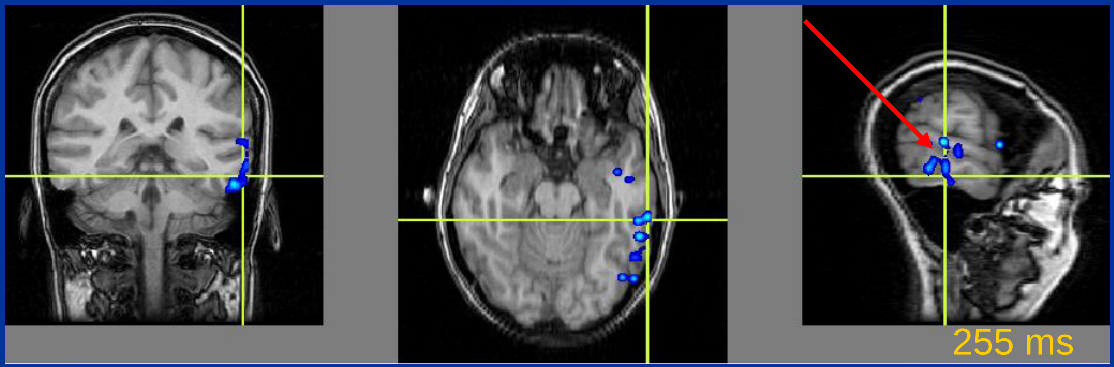
MR-FOCUSS imaging in right handed, 40 year old subject with Dysphonetic dyslexia. Superior temporal gyrus on the left side is active in the real word task but AG is active in the nonsense words. Not shown: Inferior frontal gyrus is more active in the Right IFG during the nonsense word task.

Reader with Dyseidetic Dyslexia

A. Real word



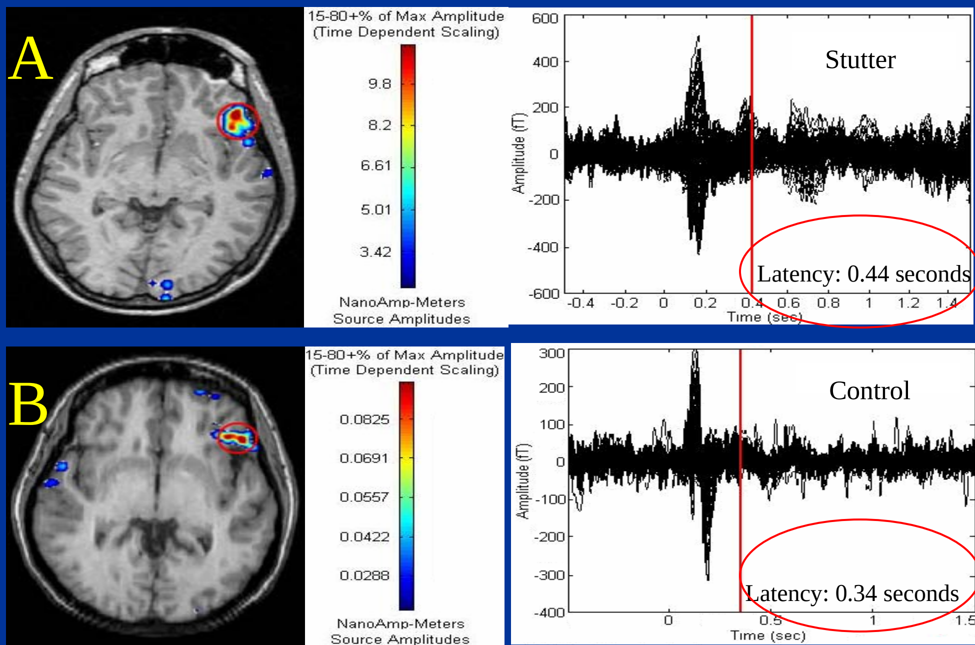
B. Nonsense word



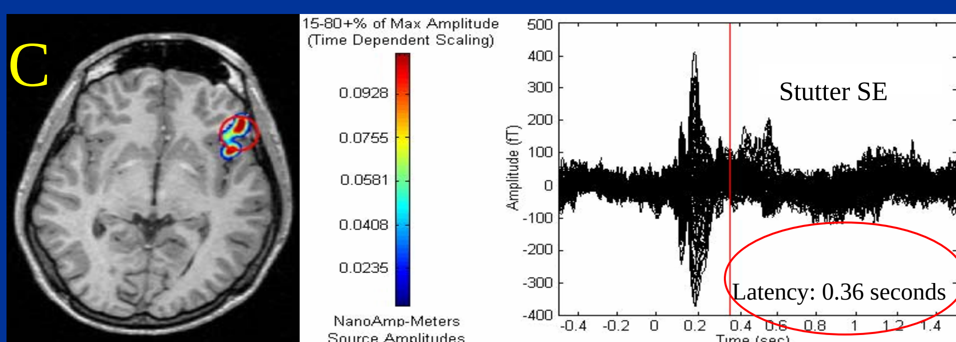
Dyseidetic subjects have problems reading whole-word non-phonologic spellings such as ‘light’ or ‘yacht

MR-FOCUSS imaging in right handed, 43 year old subject with Dyseidetic dyslexia. AG is active during real word reading but Superior and inferior temporal gyrus on the left side is active in the nonsense word reading task. This is opposite from the dysphonetic subject. Not shown: Inferior frontal gyrus is more active in the Right IFG during the real word task again opposite to the subjects with Dysphonetic dyslexia.

Patients Who Stutter



With TREATMENT



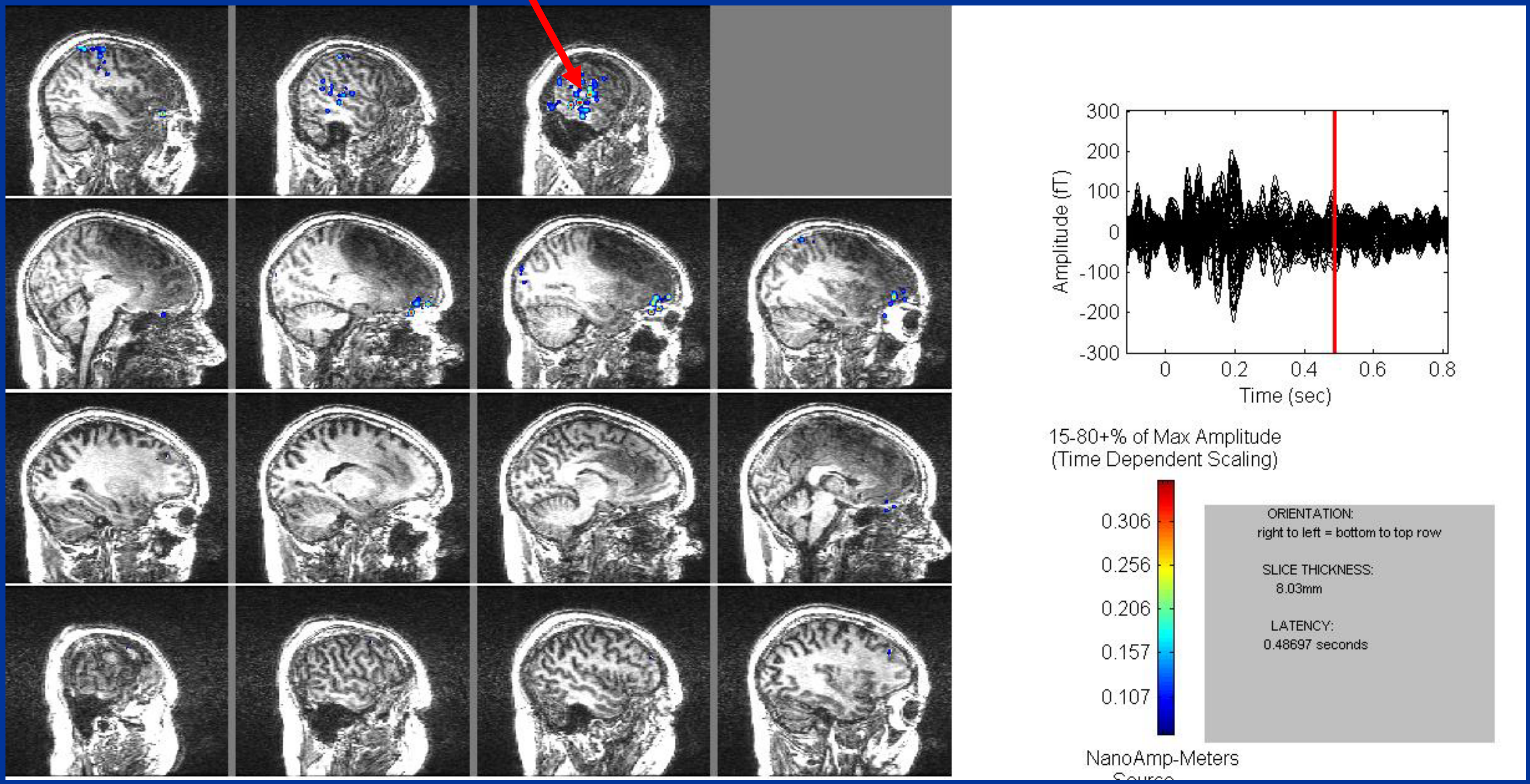
MR-FOCUSS results during verb generation Language task. Scale in nanoAmp-Meters. Broca’s area (Brodmann’s Area 45) is indicated by a red circle.

A) SWS **without** SpeechEasy®. Maximum amplitude of activation shown on bar scale is 9.8 nanoAmp-Meters. Large, visible peak on graph at latency 0.4404 seconds signifies Broca’s area activation.

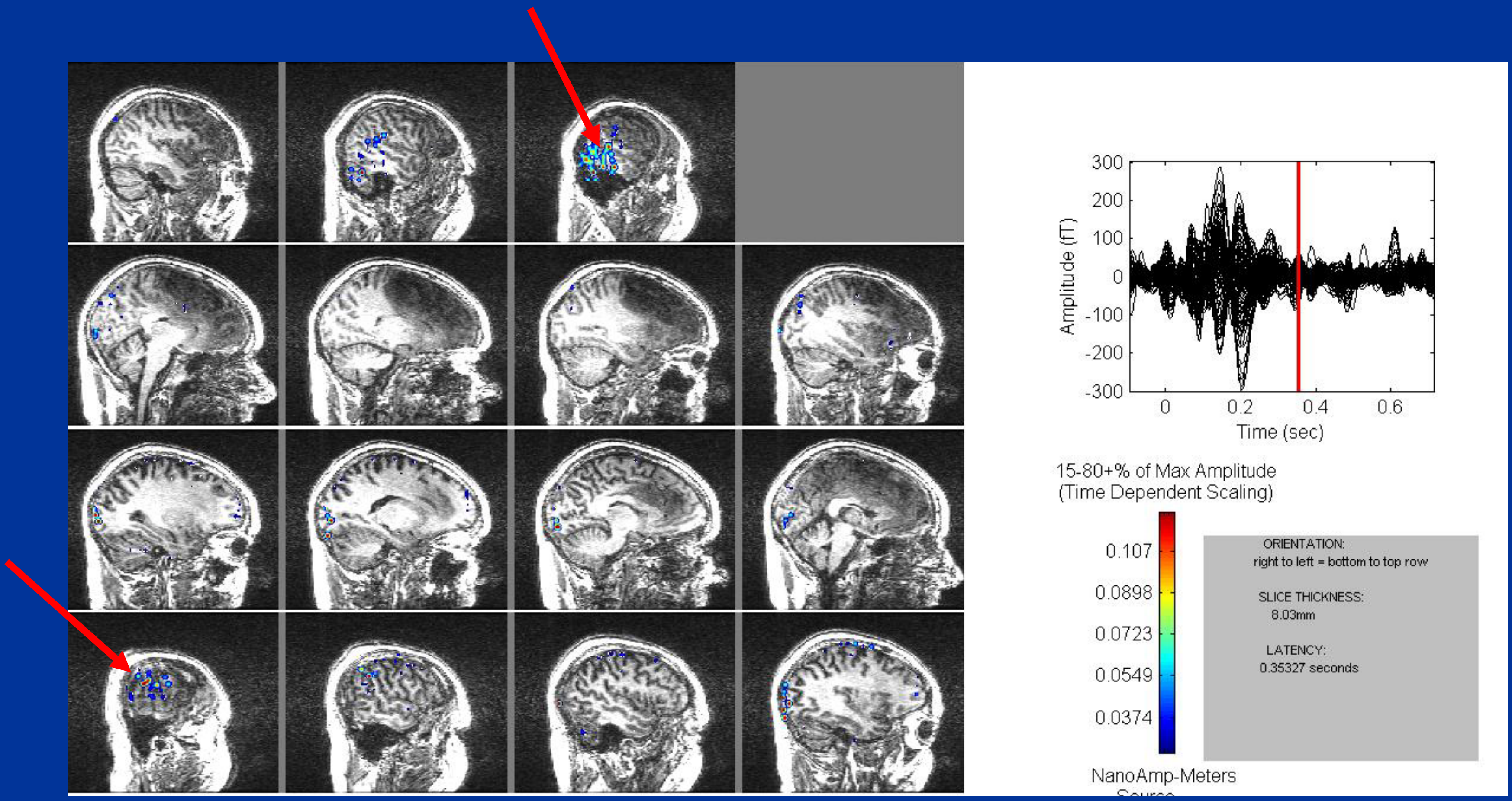
B) Control Subject. Maximum amplitude of activation is 0.0825 nanoAmp-Meters—drastically less than the stuttering patient’s. Peak on graph at latency 0.33586 seconds. Comparing latencies between the two patients, the stuttering patients showed noticeably later Broca’s area activation.

C) SWS **with** SpeechEasy®. Amplitude and latency closely matches those of the control patient, indicating that SpeechEasy® is relatively effective in treating stuttering.

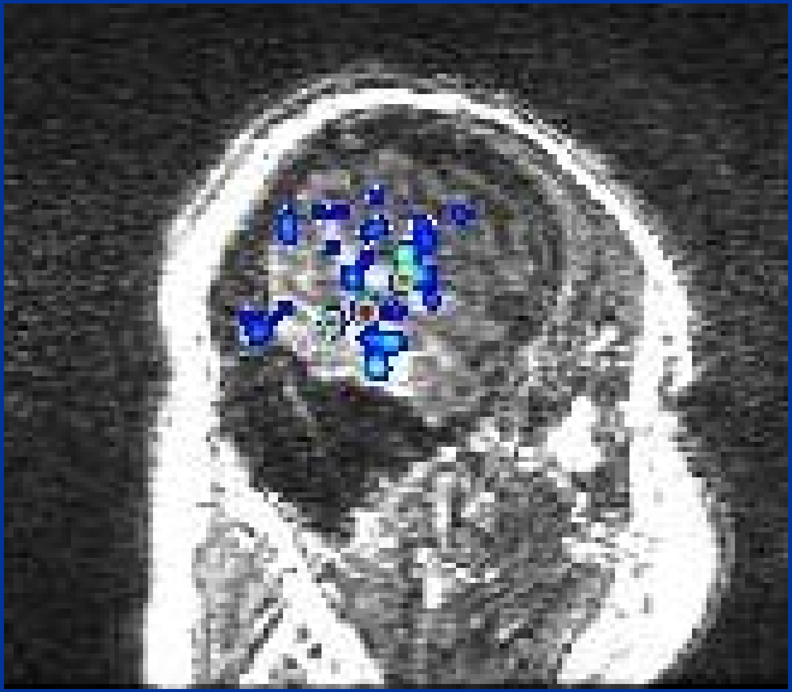
Tumor patient
Broca's area Picture naming



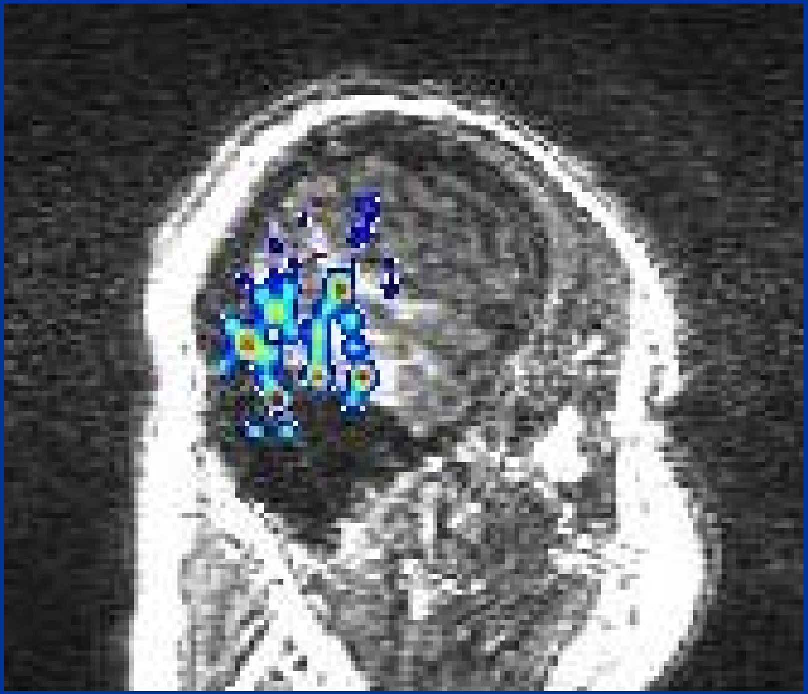
Tumor patient
Wernicke's area Verb generation



Broca's areas



Wernicke's area



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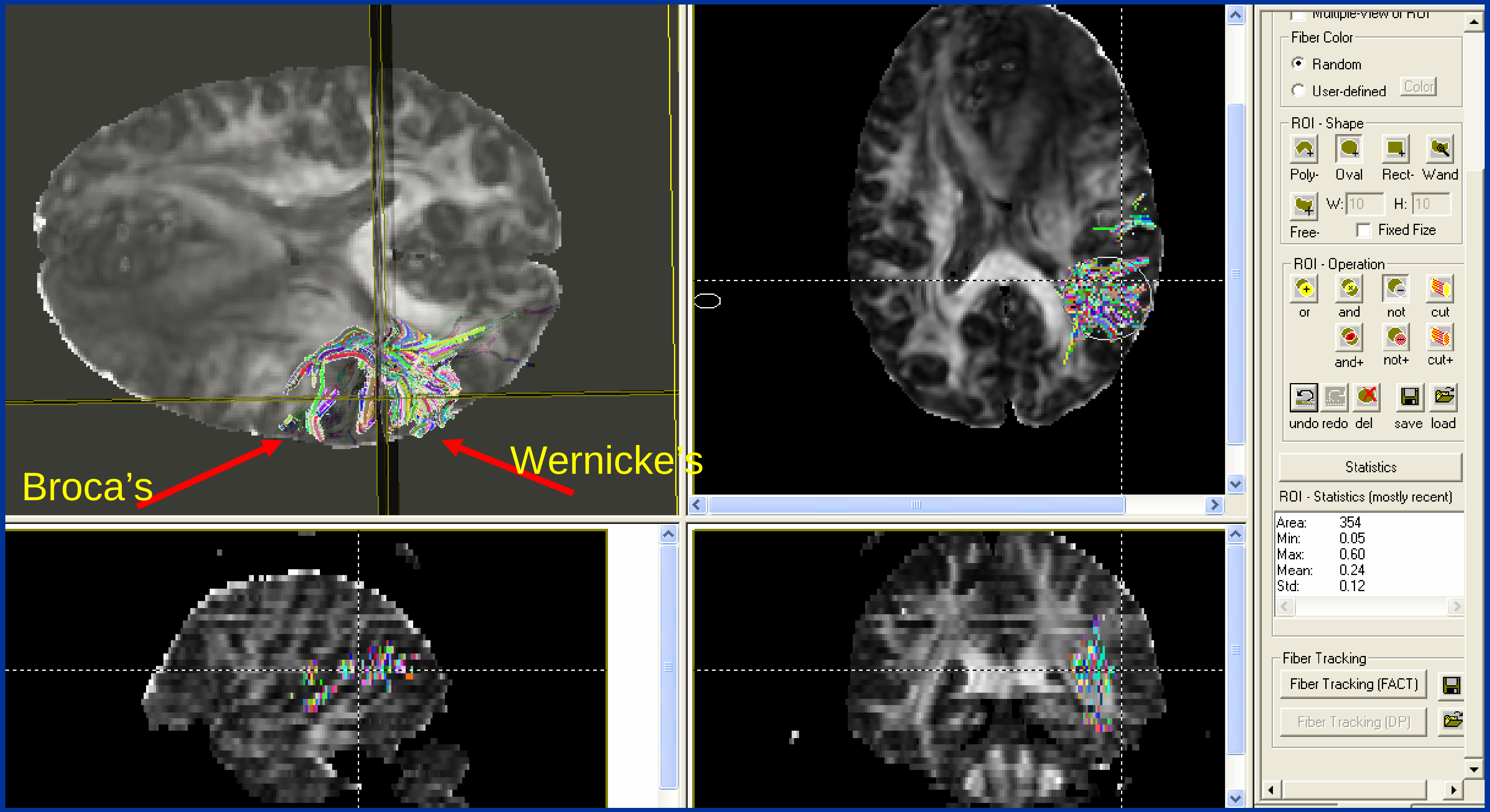
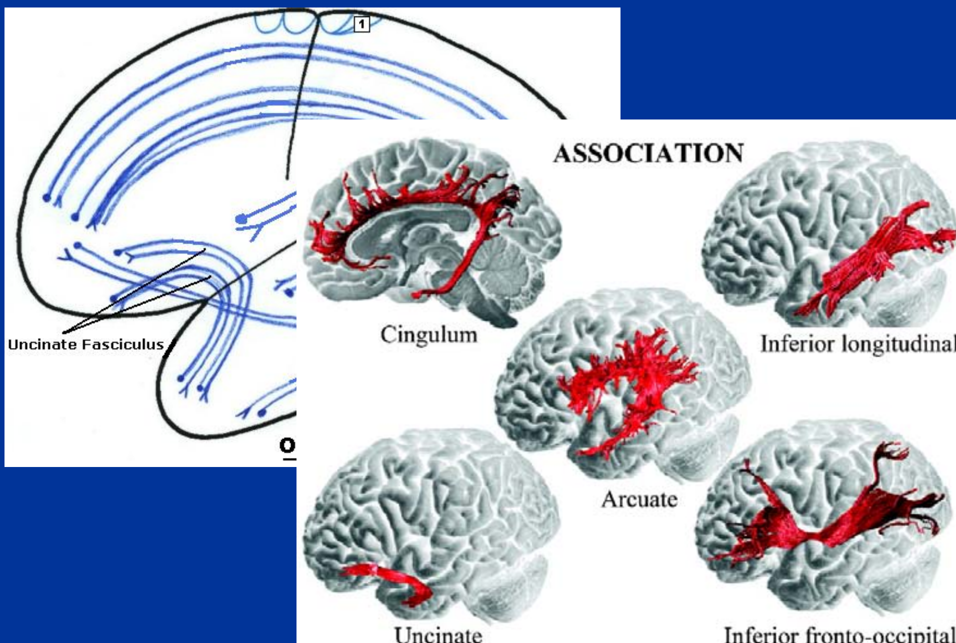
DTI Imaging

AF Fibers connecting Wernicke's and Broca's on FA Map



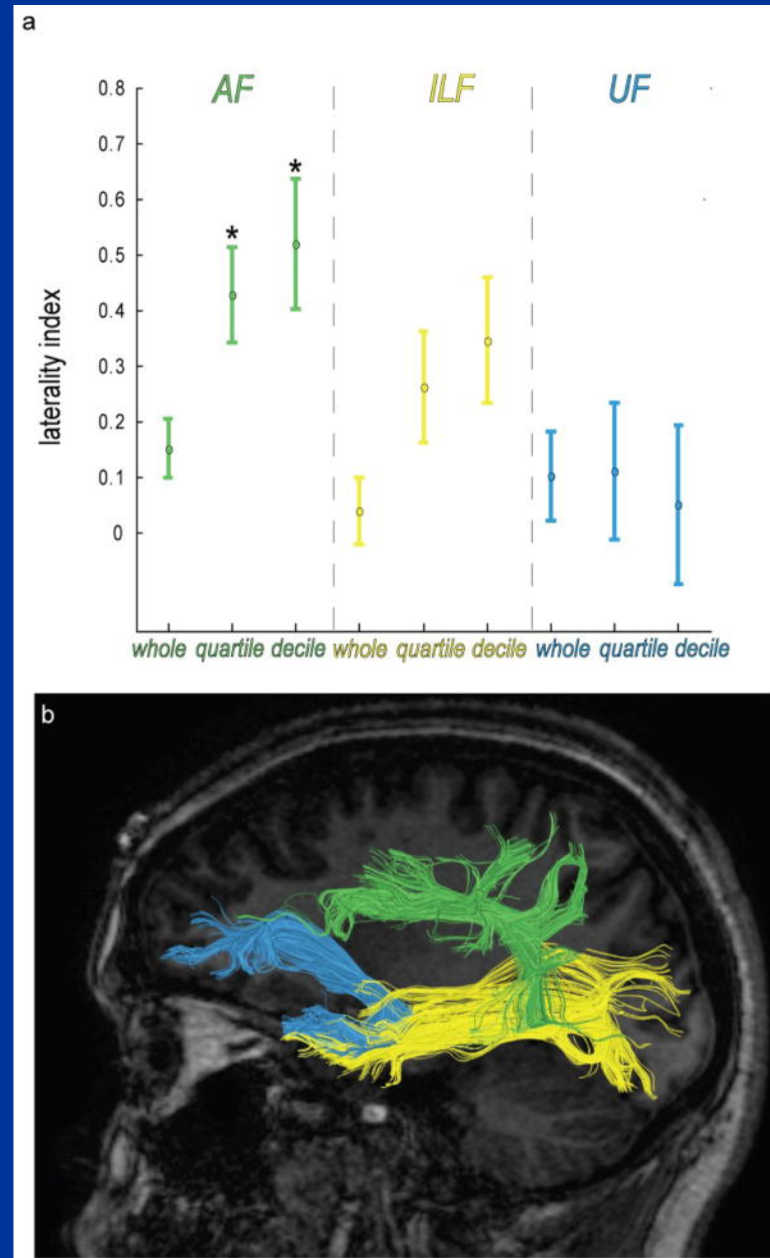
White matter tracts
visualized with diffusion tensor tractography



Catani M , ffytche D H Brain 2005;128:2224-2239

AF classified 22 of 23 (95.6%) patients language dominance correctly according to their Wada score.

Ellmore NeuroImage 2010



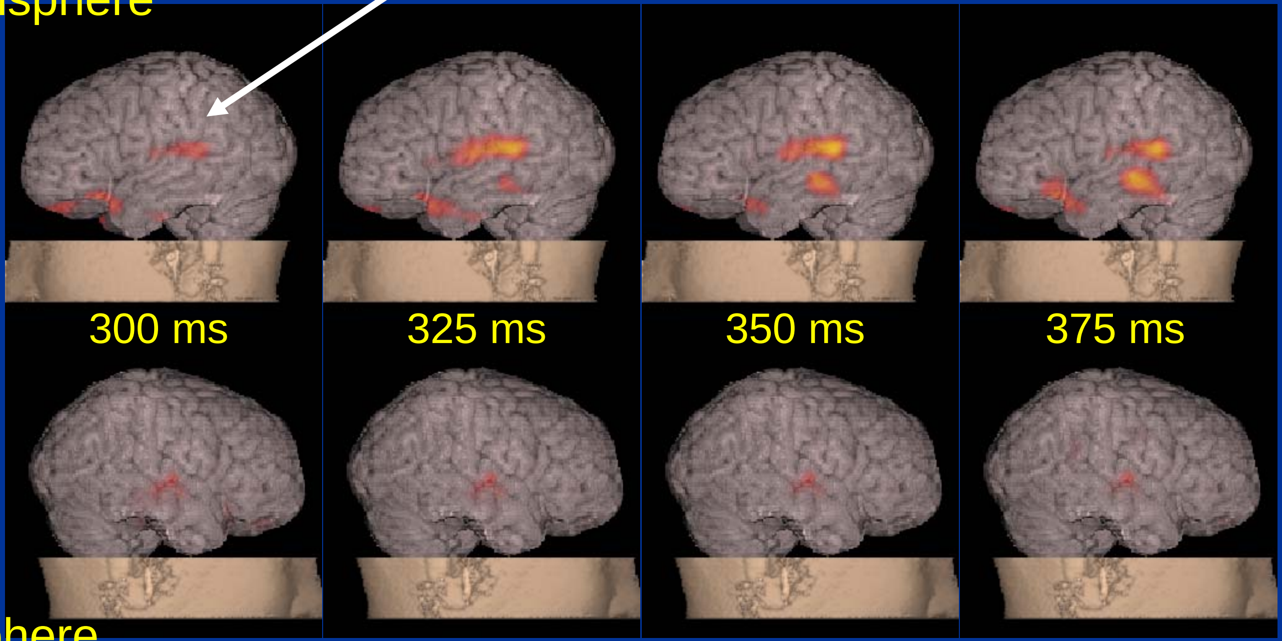
Beam Formers

- A beamformer is a set of spatial filter that linearly integrate information over multiple spatially distributed sensors.
- The basic principle of beamformer design is to allow the neuronal signal of interest to pass through in certain source locations and orientations, called pass-bands, while suppressing noise or unwanted signal in other source locations or orientations, called stop-bands.
- All existing beamformers in the EEG and MEG literature are narrow-passing-band beamformers, in which either the entire brain volume or just the cortical surface is divided into a grid of dipoles, and at each grid node, the beamformer allows signal from that node to pass and suppress signal/noise from other nodes.
- Beamformers localizes <u>Uncorrelated</u> Brain activity.
- Two Types - Scalar and Vector beamformers
- The beamformer approaches were originally developed as signal processing methods to detect signals using receptor arrays in acoustic and radio signals (Finding Submarines).

Robinson & Verba, Biomagnetism proceedings,1999

Huang et al, Brain Topography, 2004

Beamformer analysis of Language during passive reading

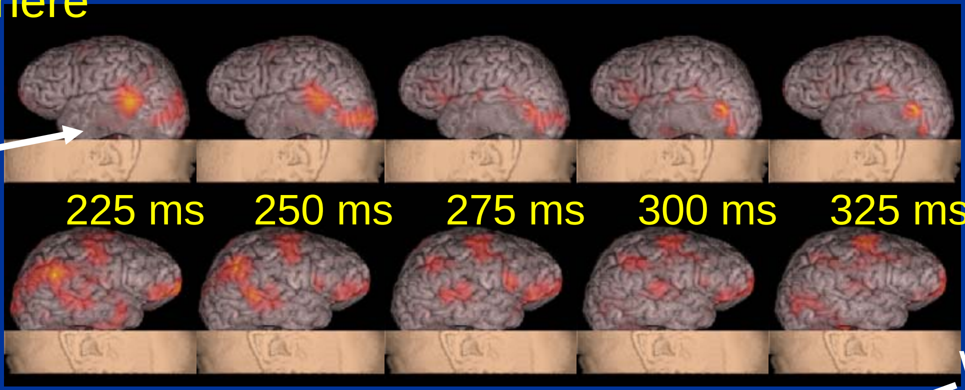


Passive listening to individual words. Each frame represents event-related activity integrated over a 50 ms time window. The time window was advanced in increments of 25 ms. In the passive listening task, activation can be seen in Wernicke's area, starting at about 300 ms. The language-related activations are seen mainly in the left hemisphere (Scale in pseudo Z-scores). Linearly constrained minimum variance (LCMV) Beamformer

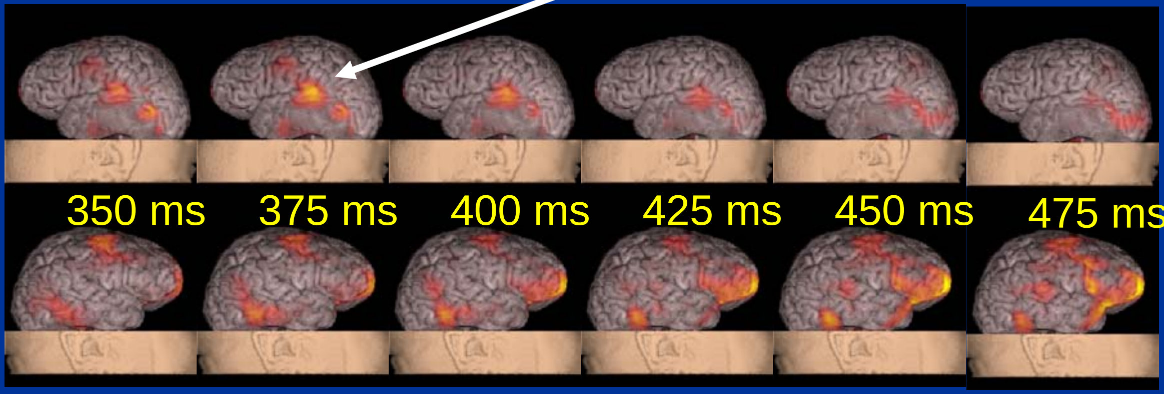
Beamformer analysis of Language during picture naming

Left Hemisphere

Tumor



Wernicke's Area

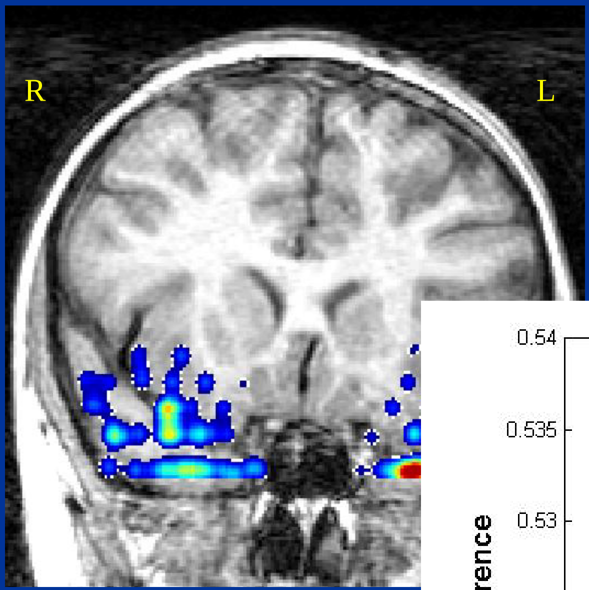


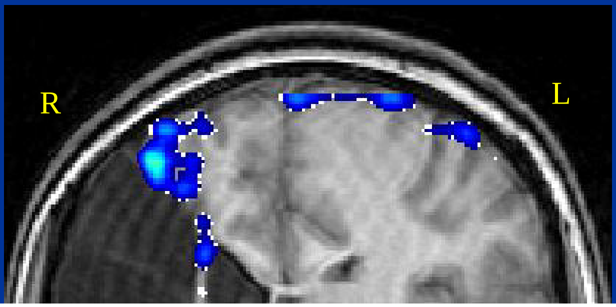
For a picture naming task, this tumor patient has a lesion occupying much of the left temporal lobe. Although activation appears in Wernicke's area, starting at about 350 ms, there is considerable activity that persists in the right hemisphere (Scale in pseudo Z-scores). Linearly constrained minimum variance (LCMV) Beamformer

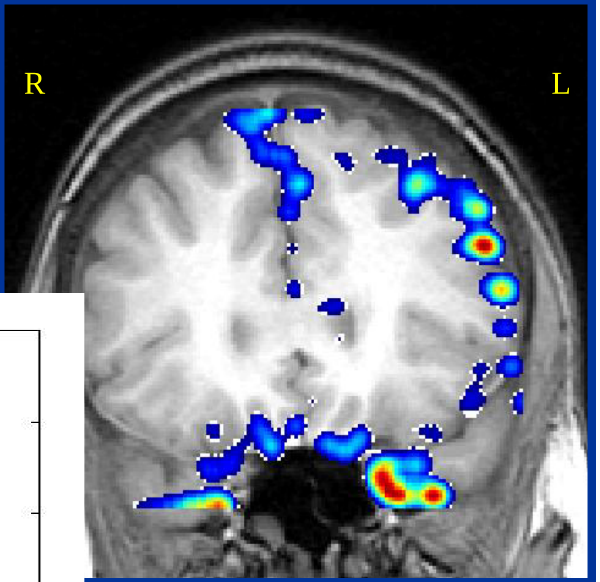
Coherence

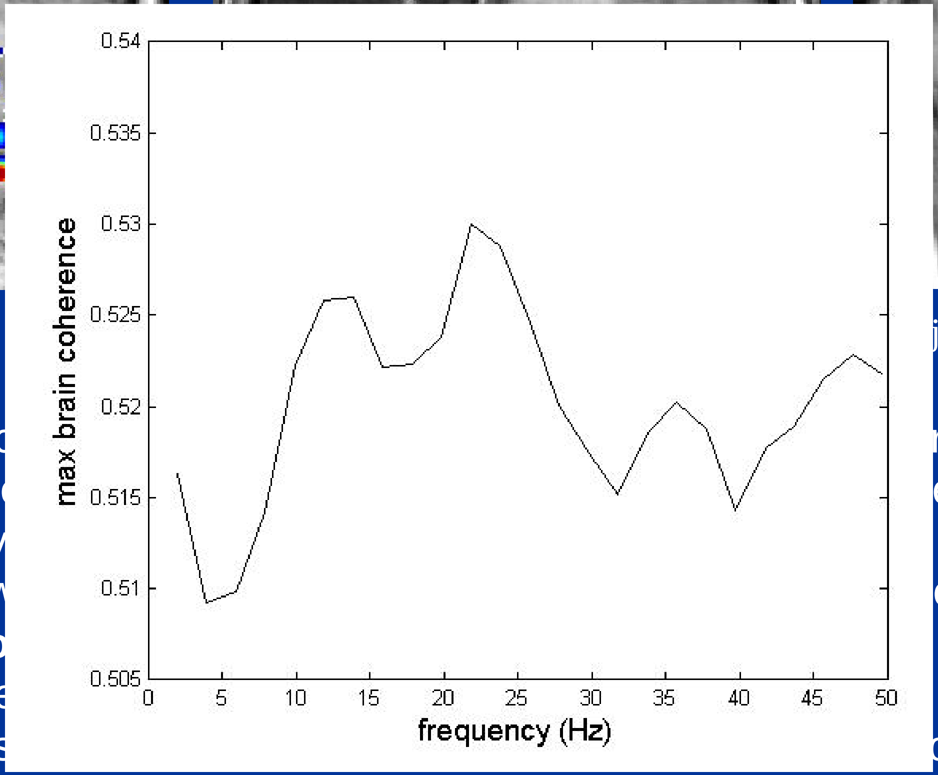
- Measures consistency of phase between cortical sites participating in a neuronal network
- Neural networks have multiple harmonic activation modes (10 Hz mode, 20 Hz mode, 35 Hz mode)
- Cortical sites participate in multiple modes and networks
- Imaged Coherent activity at each site (source) is a mixture of independent signals.
- Unlike Coherence at the MEG array (sensor) level which is a mixture of brain activity from a large volume of the brain.
- Coherence reflects the degree of information flow between groups of neurons.

Epilepsy Patients





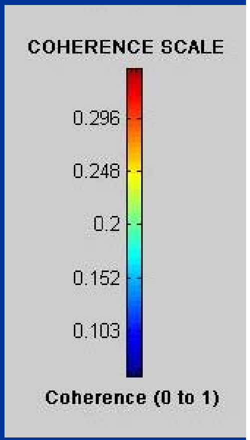




Subject #1: Left temporal

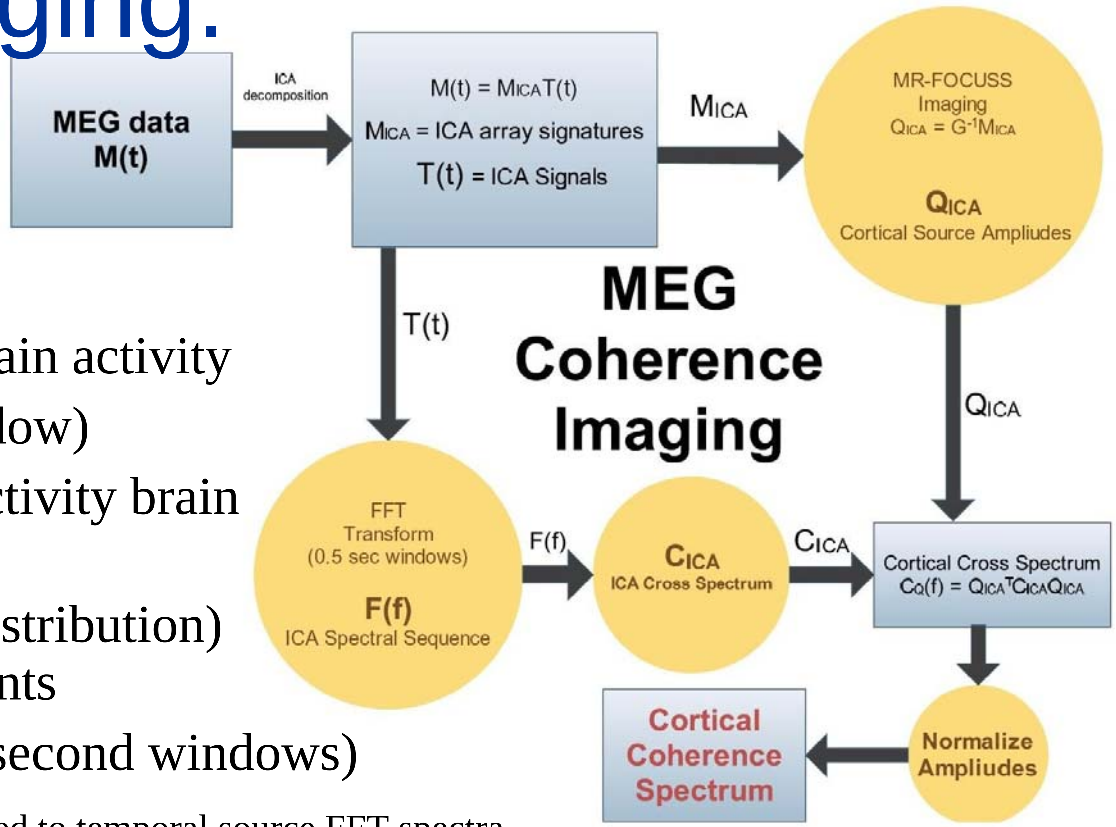
ject #7 Left temporal resection

- Increased coherenc rea of resection in 19/24 t eizure-free longer than 1 y coherence values w esected.
- 5/6 cases with a **no** coherence measure
- Coherence analysis outcomes of 77% (23/30 cases). Sensitivity of the coherence method 73% with a positive predictive value of 70% for an Engel class Ia outcome.



Elisevich et al, Epilepsia, 2011

Coherence Imaging: Calculation



1. Calculate time sequence of brain activity (divide data into 7.5 sec window)
   a. ICA extraction of burst activity brain source signals
   b. MR-FOCUSS (current distribution) imaging of ICA components
2. Calculate FFT sequence (0.5 second windows)

   temporal sequences of sources are converted to temporal source FFT spectra
3. Calculate cross-spectral matrix between sources (ICA components) for each frequency
4. Calculate coherence between all network structures
5. For each active cortical site the average coherence with all other sources is calculated for each frequency.
6. Both the Imaginary and Real components are incorporated in the coherence imaging results.

Moran, Biomag, 2006

Extracting real-time neural networks from MEG data

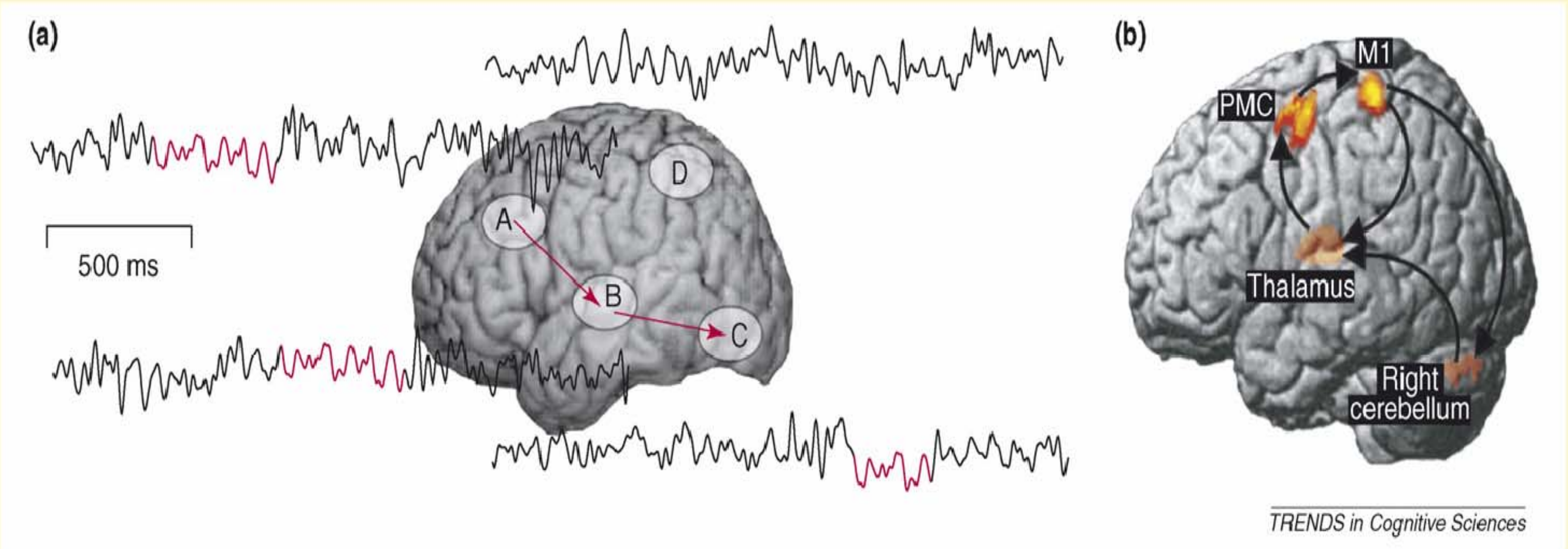
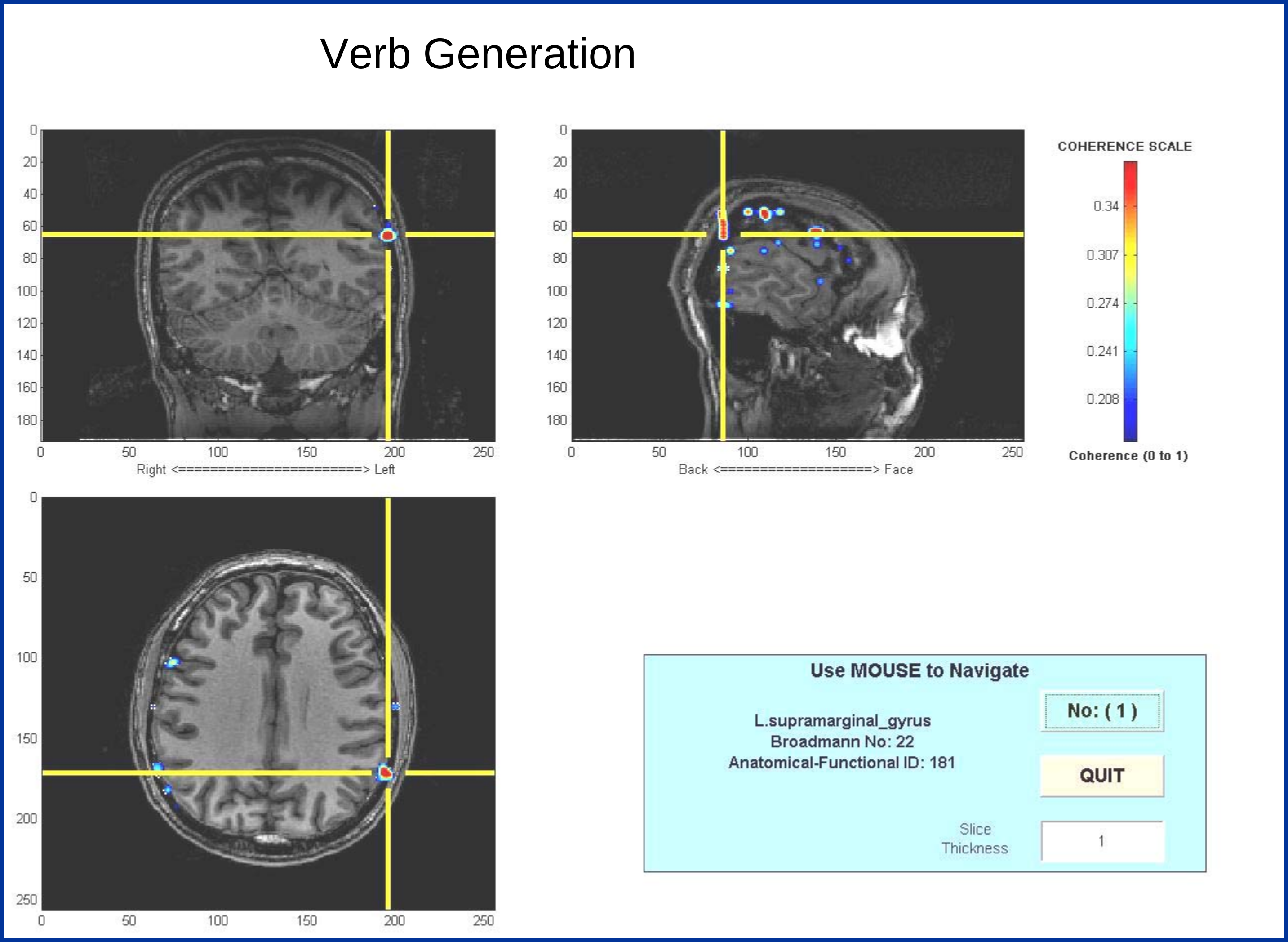


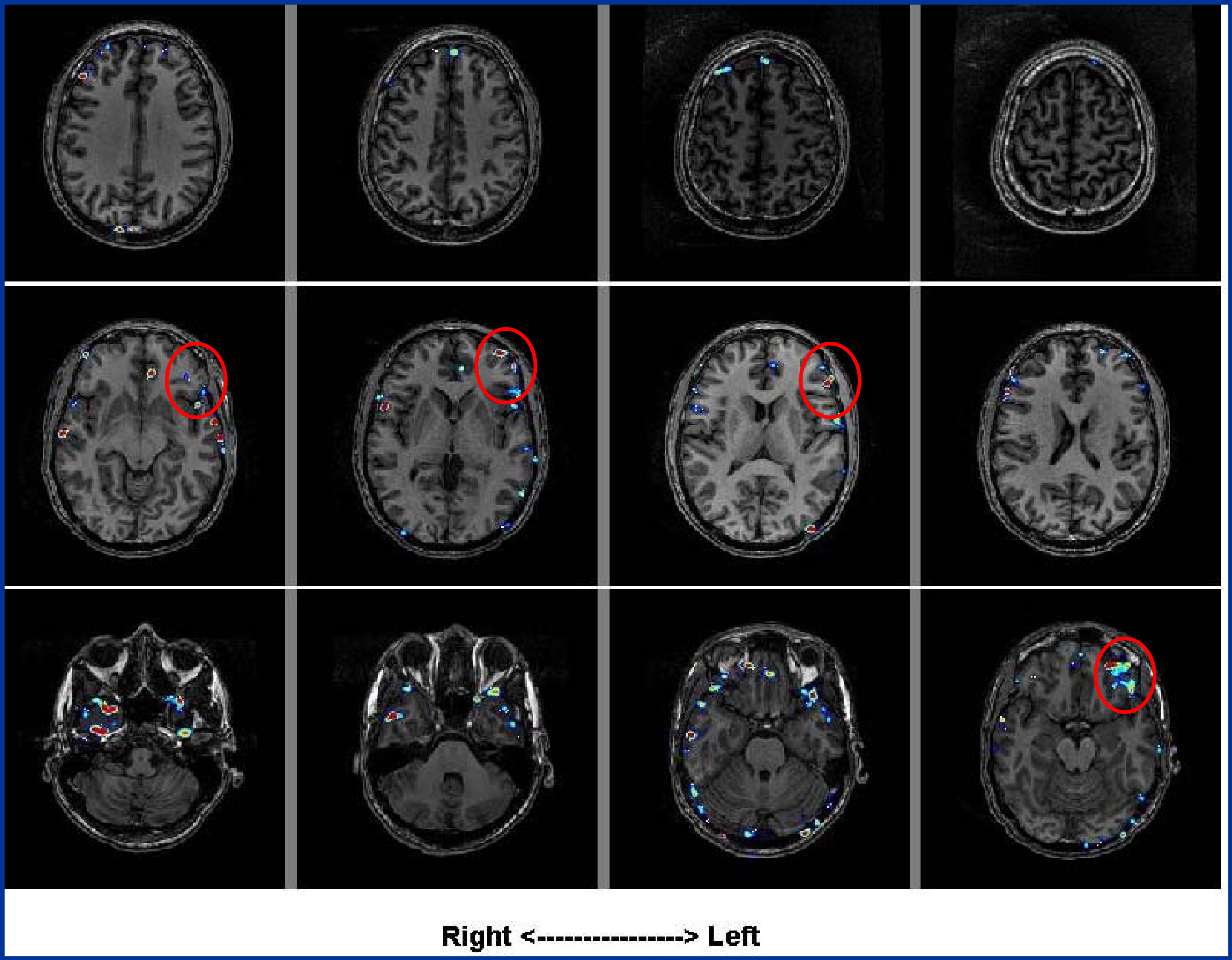
Figure I. Extracting long-range neural connectivity from MEG data. **(a)** Simplified presentation of the basic idea. Curves depict time courses of activity in four brain areas (gray ellipses). If neuronal populations in these areas are functionally connected, one would expect to detect similar time 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].

Gross J, et al Proc Natl, Acad Sci. 2002

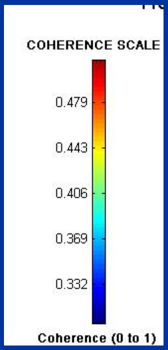
Coherence for language localization in Normal Readers



Coherence for language localization in Normal Readers



Picture Naming
Left Inferior Frontal gyrus
BA 45 also 47 and 11



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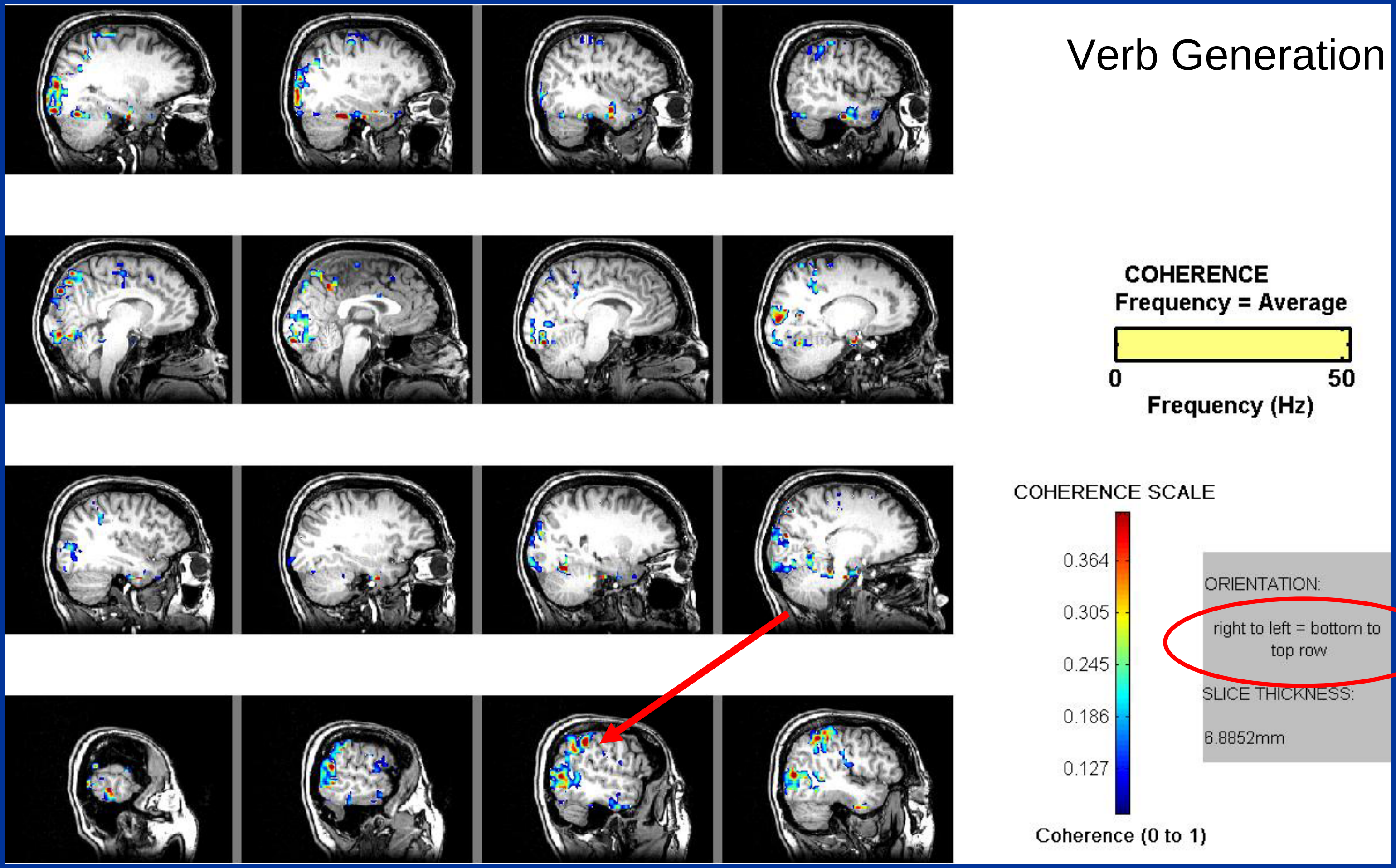
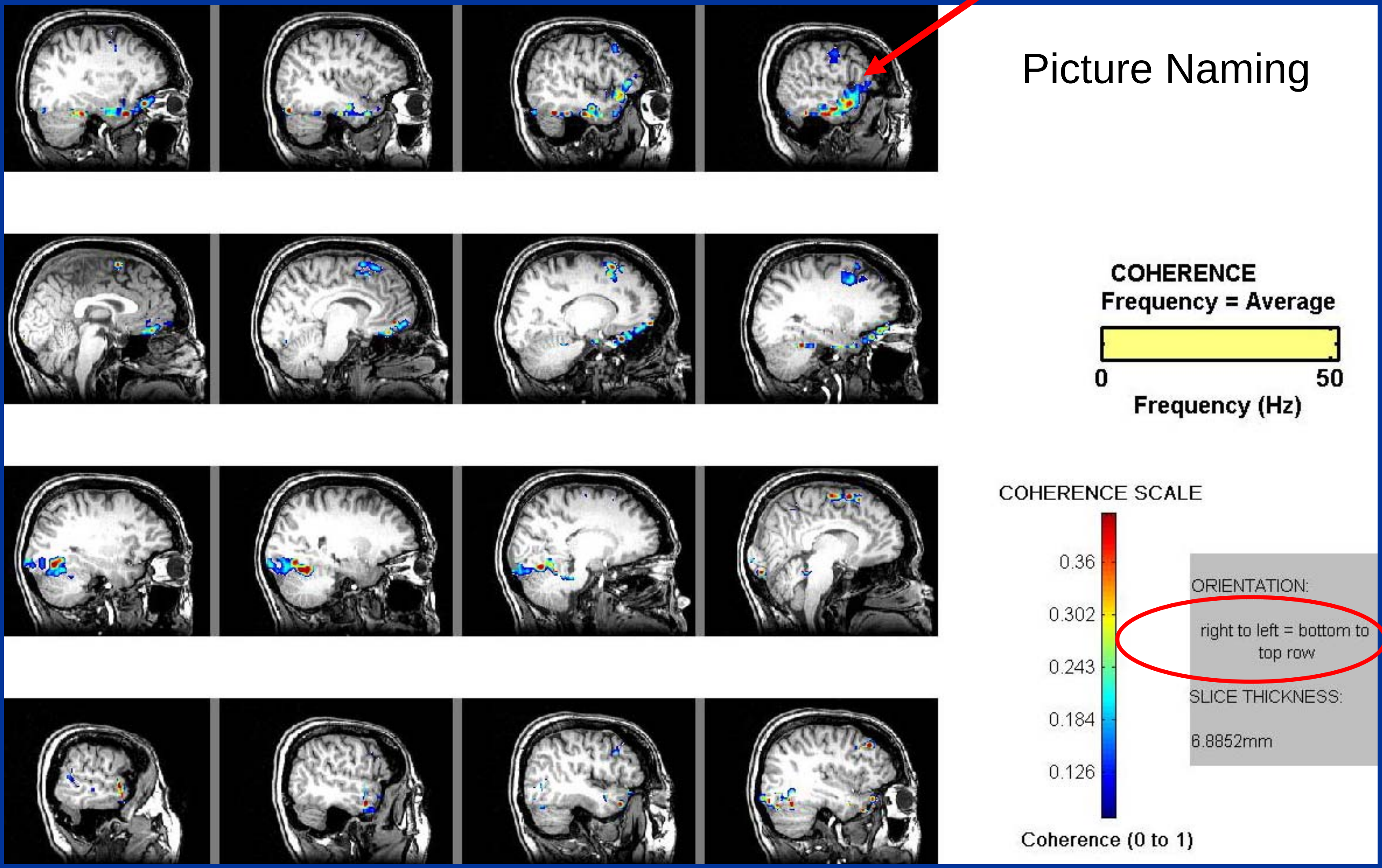
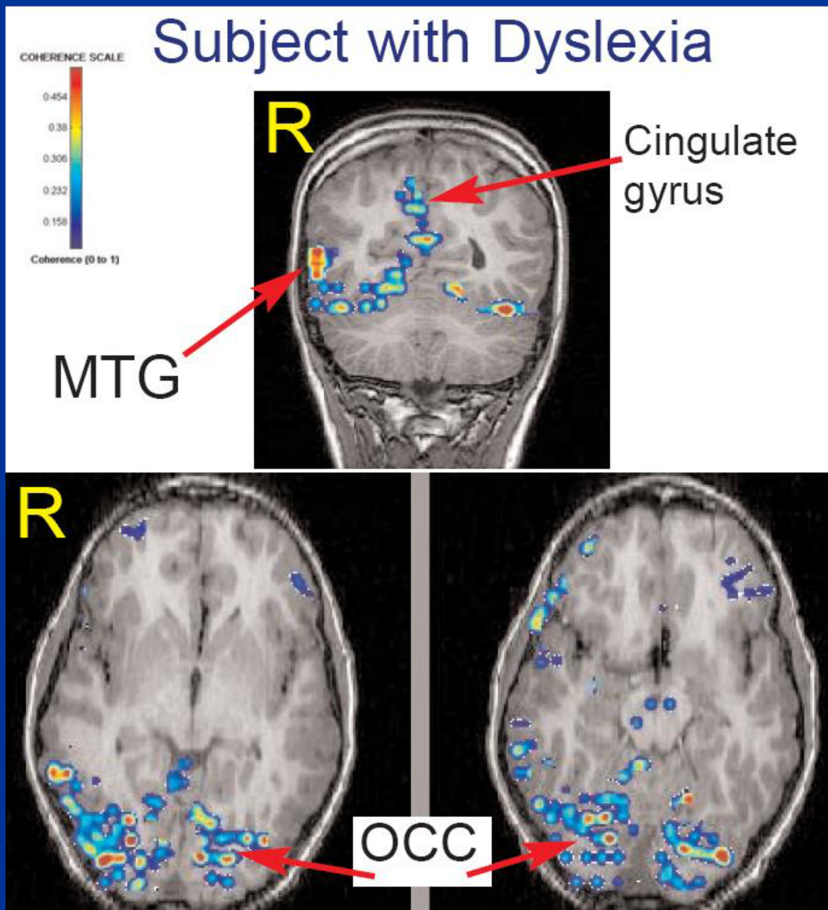
Wernicke's in Epilepsy patient
Coherence imaging

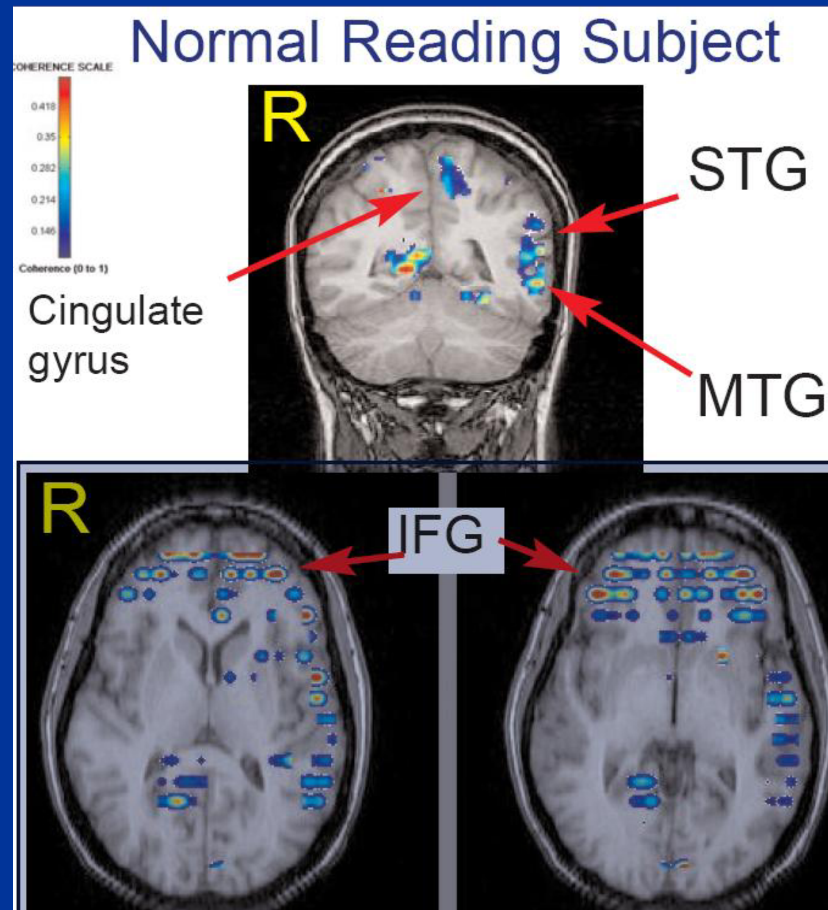


Broca's in Epilepsy patient Coherence imaging



Dyslexia





Dyslexic Subject displayed more highly coherent regions (red) in the occipital lobe than normal readers. Also the middle temporal gyrus (MTG) in the RIGHT hemisphere has more coherence than LEFT hemisphere.

Normal Reading Subject displayed more highly coherent regions in the inferior frontal gyrus than subjects with dyslexia. Also the MTG in the LEFT hemisphere had more coherent activity than the RIGHT hemisphere.

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Summary

- There are several functional imaging techniques that are a safe and non-invasive to image neural function of language processes. (Multimodal integration)
- fMRI and PET provide millimeter spatial resolution for language localization.
- MEG provides millimeter spatial resolution PLUS millisecond temporal resolution needed to understand language processing steps.
- Utilizing Advance imaging techniques beyond ECD provides an expanded view of the regions of the brain that are concurrently involved in language processing.

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- Norman Tepley Physicist and Lab Director
  Henry Ford Hospital

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