Brain Connectivity Measures: Application to Epilepsy Networks

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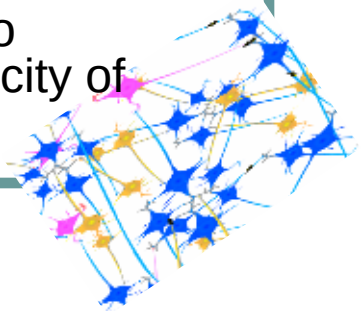
1915

Our Summary

- **Need:** What do clinicians want to know from brain imaging.

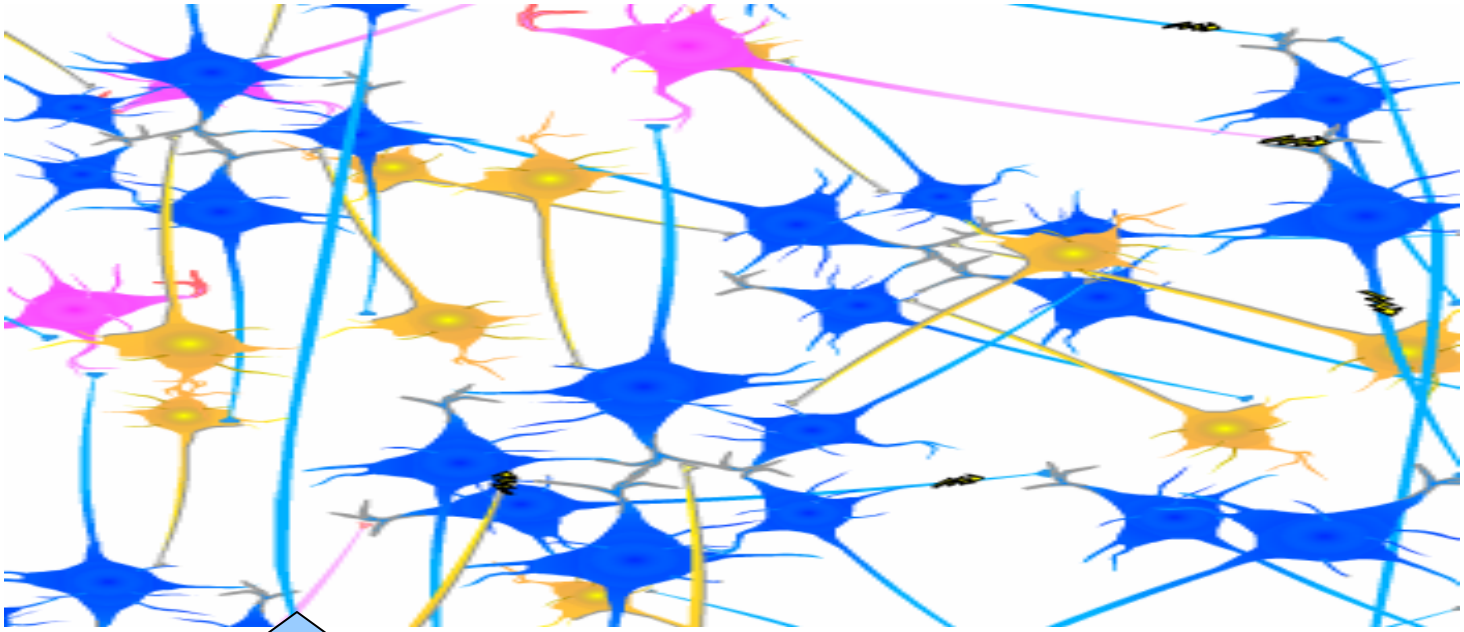
  Where is the epileptogenic zone!

- **Why:** Can we predict the best location to perform a surgical resect that will provide an optimum outcome for each patient.
- **Questions:** The hypothesis is that highly coherent brain regions are more probably the epileptogenic zone in patients with epilepsy.
- **Tools and Techniques:** Noninvasive MEG, 148 magnetometers, Filter 3-50Hz, clean the 10 minute resting state data. Identify the areas in the brain that are communicating with each other with Coherence then apply Granger Causality to determine direction of information flow.
- **Discovery:** We find that the patients with epilepsy have a very well connected brain that is highly communicative (synchronized).
- **Implications:** Do we just take the senders or do we need to identify the receivers and take both? What happens with plasticity of the brain if we did not remove all the epileptogenic activity?

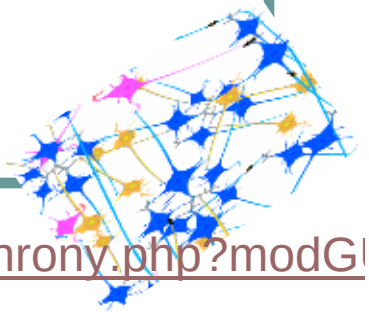


Neuronal Synchrony

- What do we mean by synchrony



Start video

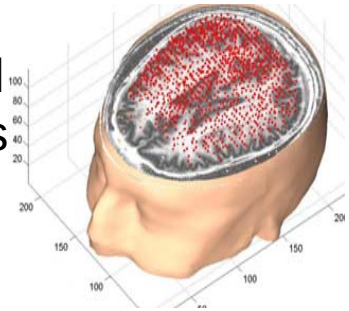


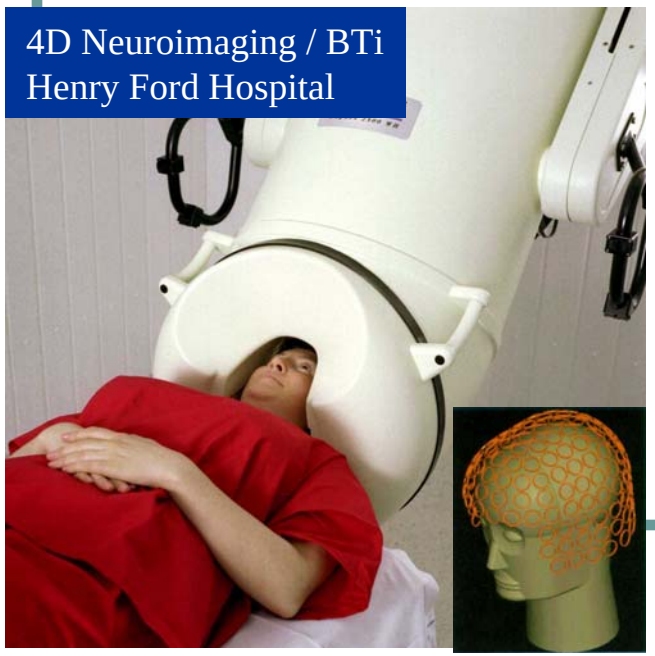
- http://www.mind.ilstu.edu/curriculum/neural_synchrony/neural_synchrony.php?modG

Tools and Techniques

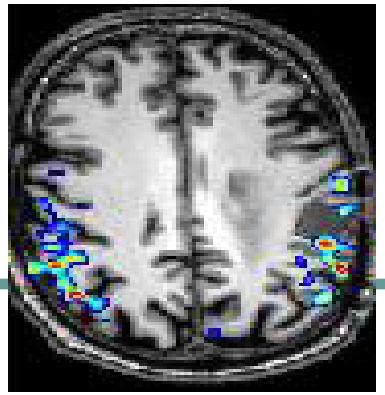
- Archival review of 57 presurgical patients with MEG coherence source imaging (CSI) studies from 10 minutes of spontaneous brain activity.
- Location of most Persistent cortical site, Sending and Receiving brain regions determined by Granger causality analysis of the MEG-CSI solution.
- Compared to surgically resected brain areas.
- ILAE and Engel outcome classifications were assessed using nonparametric tests.

Source Model
~4000 dipoles

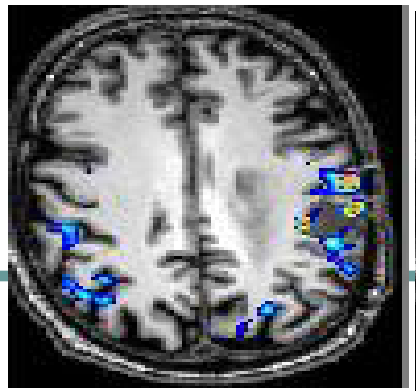




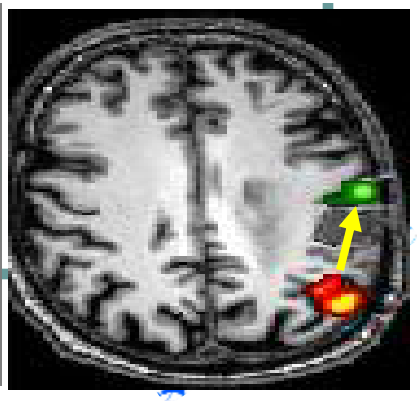
Coherence



Persistence



Sending (Red)
Receiving (Green)
Granger Causality



Coherence networks in Epile

- **Sou … tomical loca…**
  - Increase… concorda…
  - Coheren… 70% for … a predict…

Epilepsia, **(*):1–10, 2011
doi: 10.1111/j.1528-1167.2011.02990.x

FULL-LENGTH ORIGINAL RESEARCH

An assessment of MEG coherence imaging in the study of temporal lobe epilepsy

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SUMMARY

Purpose: This study examines whether magnetoencephalographic (MEG) coherence imaging is more sensitive than the standard single equivalent dipole (ECD) model in lateralizing the site of epileptogenicity in patients with drug-resistant temporal lobe epilepsy (TLE).

Methods: An archival review of ECD MEG analyses of 30 presurgical patients with TLE was undertaken with data extracted subsequently for coherence analysis by a blinded reviewer for comparison of accuracy of lateralization. Postoperative outcome was assessed by Engel classification. MEG coherence images were generated from 10 min of spontaneous brain activity and compared to surgically resected brain areas outlined on each subject's magnetic resonance image (MRI). Coherence values were averaged independently for each hemisphere to ascertain the laterality of the epileptic network. Reliability between runs was established by calculating the correlation between epochs. Match rates compared the results of each of the two MEG analyses with optimal postoperative outcome.

Key Findings: The ECD method provided an overall match rate of 50% (13/16 cases) for Engel class I outcomes, with 37% (11/30 cases) found to be indeterminate (i.e., no spikes identified on MEG). Coherence analysis provided an overall match rate of 77% (20/26 cases). Of 19 cases without evidence of mesial temporal sclerosis, coherence analysis correctly lateralized the side of TLE in 11 cases (58%). Sensitivity of the ECD method was 41% (indeterminate cases included) and that of the coherence method 73%, with a positive predictive value of 70% for an Engel class Ia outcome. Intrasubject coherence imaging reliability was consistent from run-to-run (correlation >0.90) using three 10-min epochs.

Significance: MEG coherence analysis has greater sensitivity than the ECD method for lateralizing TLE and demonstrates reliable stability from run-to-run. It, therefore, improves upon the capability of MEG in providing further information of use in clinical decision-making where the laterality of TLE is questioned.

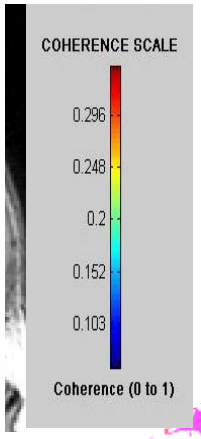
KEY WORDS: Magnetoencephalography, Interictal activity, Single equivalent current dipole, Presurgical assessment, Neuronal network.

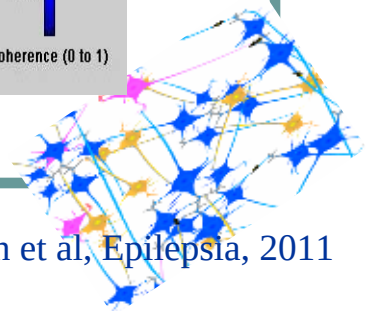
Table 3. Summary of Engel classes with ECD and MEG analyses

	ECD		Coherence analysis	
Engel class	Match[a]	No match	Match[a]	No match
Ia	9	13	16	6
Ib	1	0	1	0
Ic	1	0	1	0
Id	2	0	2	0
IIa	0	1	1	0
IIb	1	0	1	0
IIIa	2	0	1	1
Total	16	14	23	7

[a]A match indicates agreement of MEG analysis with the laterality of the surgical resection and, therefore, the result of standard investigation.

Subject



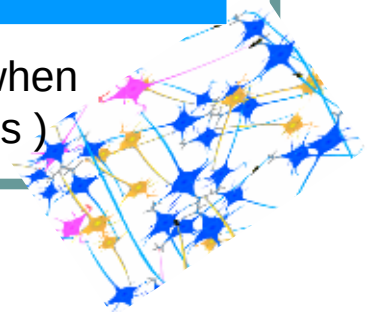


Elisevich et al, Epilepsia, 2011

Discovery: **Outcomes by RECEIVER resected status**

Variable	Response	No resection (N= 16)	Resection (N= 9)	p-value
Outcome ILAE	1	12 (75%)	3 (33%)	
	2	4 (25%)	2 (22%)	
	4	0 (0%)	3 (33%)	
	5	0 (0%)	1 (11%)	
	Mean± S.D. Median (Range)	1.25 ± 0.45 1 (1 to 2)	2.67 ± 1.58 2 (1 to 5)	0.023
Outcome Engel	1	16 (100%)	5 (56%)	
	3	0 (0%)	3 (33%)	
	4	0 (0%)	1 (11%)	
	Mean± S.D. Median (Range)	1.00 1	2.00 ± 1.22 1 (1 to 4)	0.010

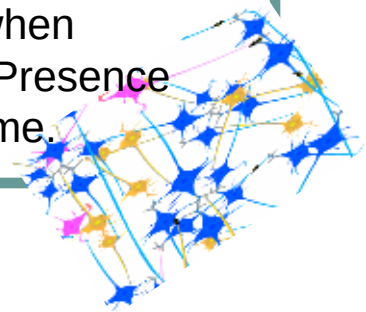
Patients with any receiver resection had on average worse outcomes when compared to patients with no receiver resection. (Pairwise comparisons)



Discovery: **Outcomes by SENDER resected status**

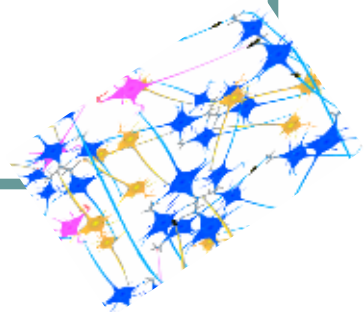
Variable	Response	No resection (N= 16)	Resection (N= 9)	p-value
Outcome ILAE	**1**	**9 (56%)**	**6 (67%)**	
	2	**5 (31%)**	**1 (11%)**	
	4	**2 (13%)**	**1 (11%)**	
	5	**0 (0%)**	**1 (11%)**	
	Mean± S.D. **Median (Range)**	**1.69 ± 1.01** **1 (1 to 4)**	**1.89 ± 1.54** **1 (1 to 5)**	**0.898**
Outcome Engel	**1**	**14 (88%)**	**7 (78%)**	
	3	**2 (13%)**	**1 (11%)**	
	4	**0 (0%)**	**1 (11%)**	
	Mean± S.D. **Median (Range)**	**1.25 ± 0.68** **1 (1 to 3)**	**1.56 ± 1.13** **1 (1 to 4)**	**0.512**

Patients with any sender resection had no significantly worse outcomes when compared to patients with no sender resection (Pairwise comparisons). Presence or absence of MRI lesion did not make any significant difference in outcome.

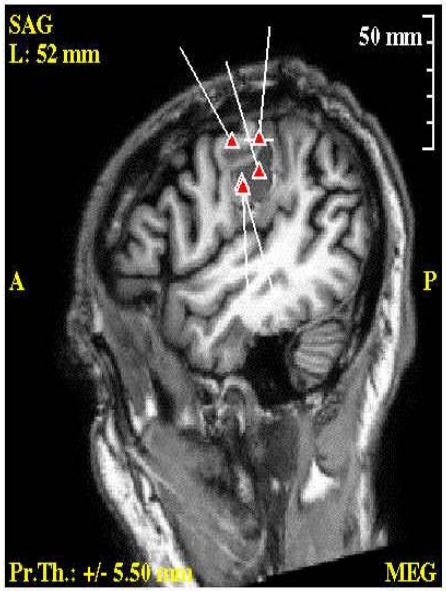


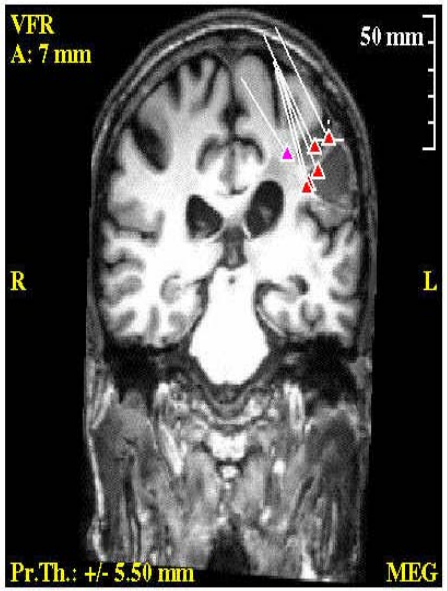
Engel 1a outcome

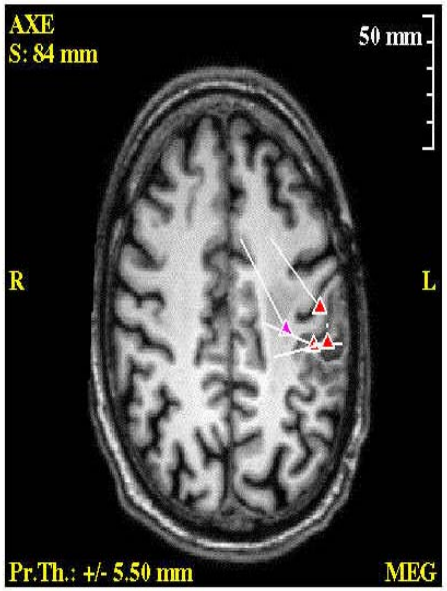
- 2861 MS
- COH sending removed and doing well.
- Location of resection- Left angular gyrus
- Engle outcome - 1a
- ILEA outcome - 1



Engel 1a MEG ECD results





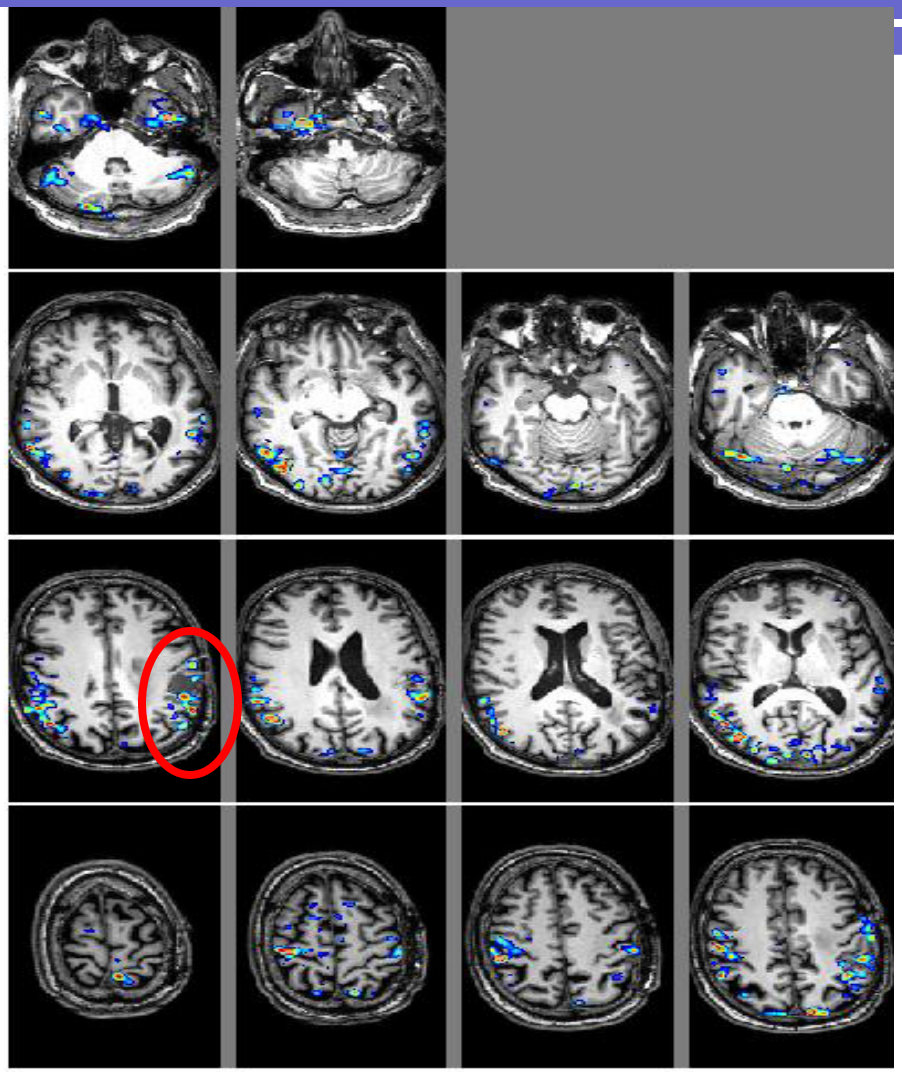


HF1s

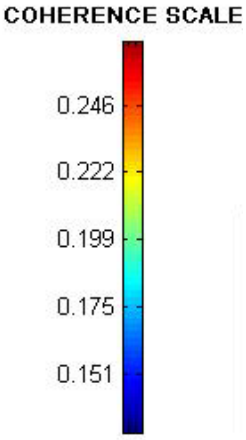
Scan :	EpiCnt1000
Session :	09/11/13 10:46
Run :	1
File : 78_c,rfDC,f1-100n4069,o,lA	
Epoch : 1	Latency : 200.529 s
Position :	(0.70, 5.24, 8.87) (cm)
Orientation :	(-9.95, -50.83, 80.21) (nAm)
||Q|| :	95.48 nAm
RMS :	680.024 fT
Conf. Vol. :	0.121329 cm^3
Correlation :	0.9906296
Good. of fit:	0.9737104
Iterations :	1

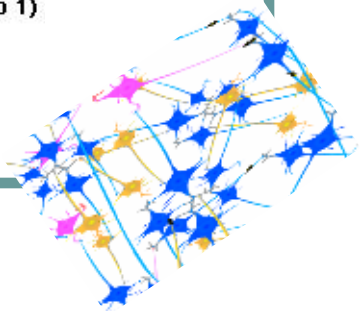
Engel 1a MEG CSI results

Coherence rest state run2



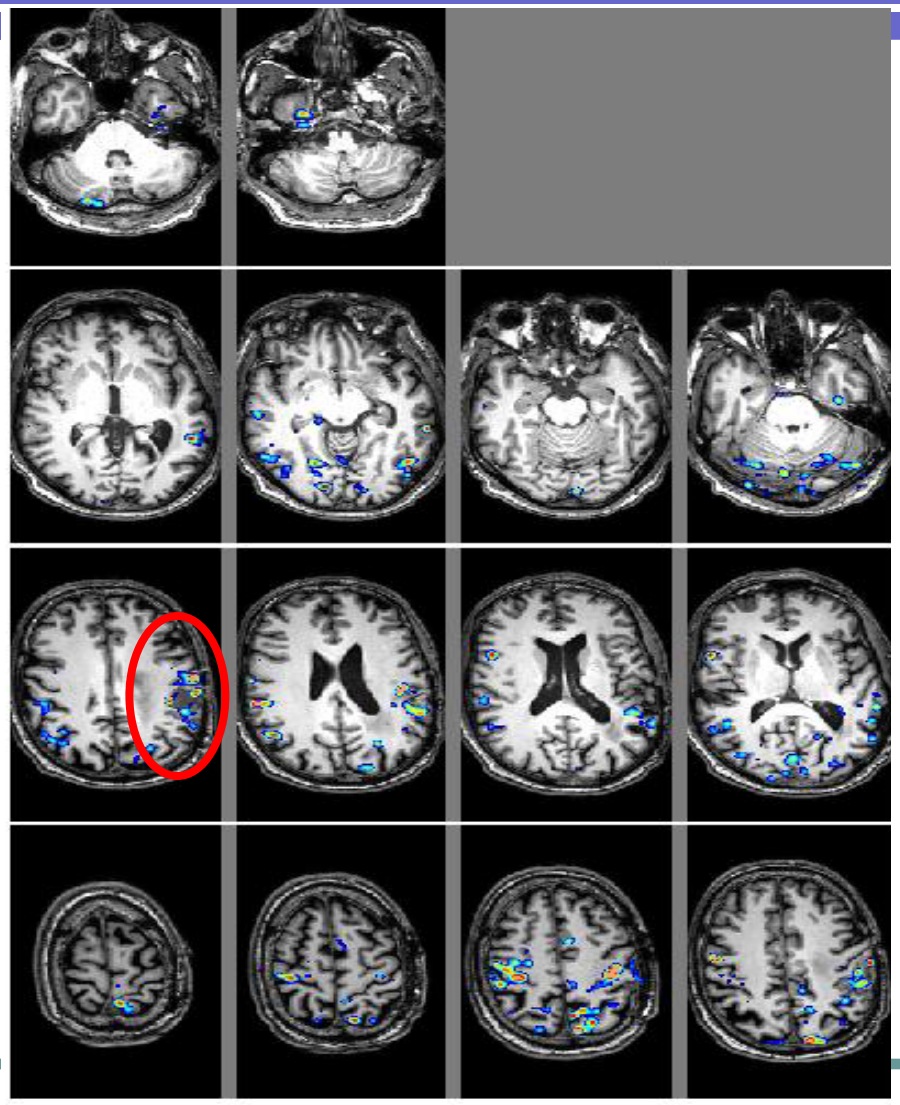
Right <----------> Left





Engel 1a MEG CSI results

Persistence rest state run2



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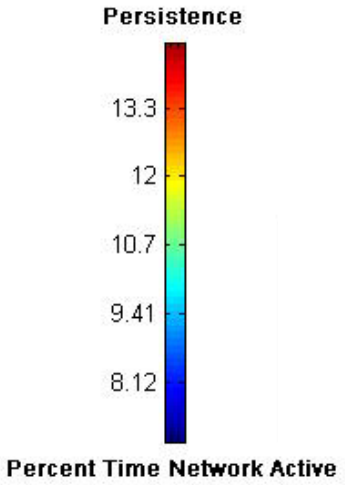
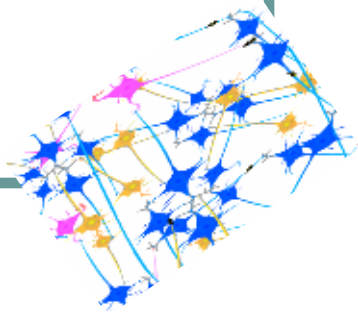
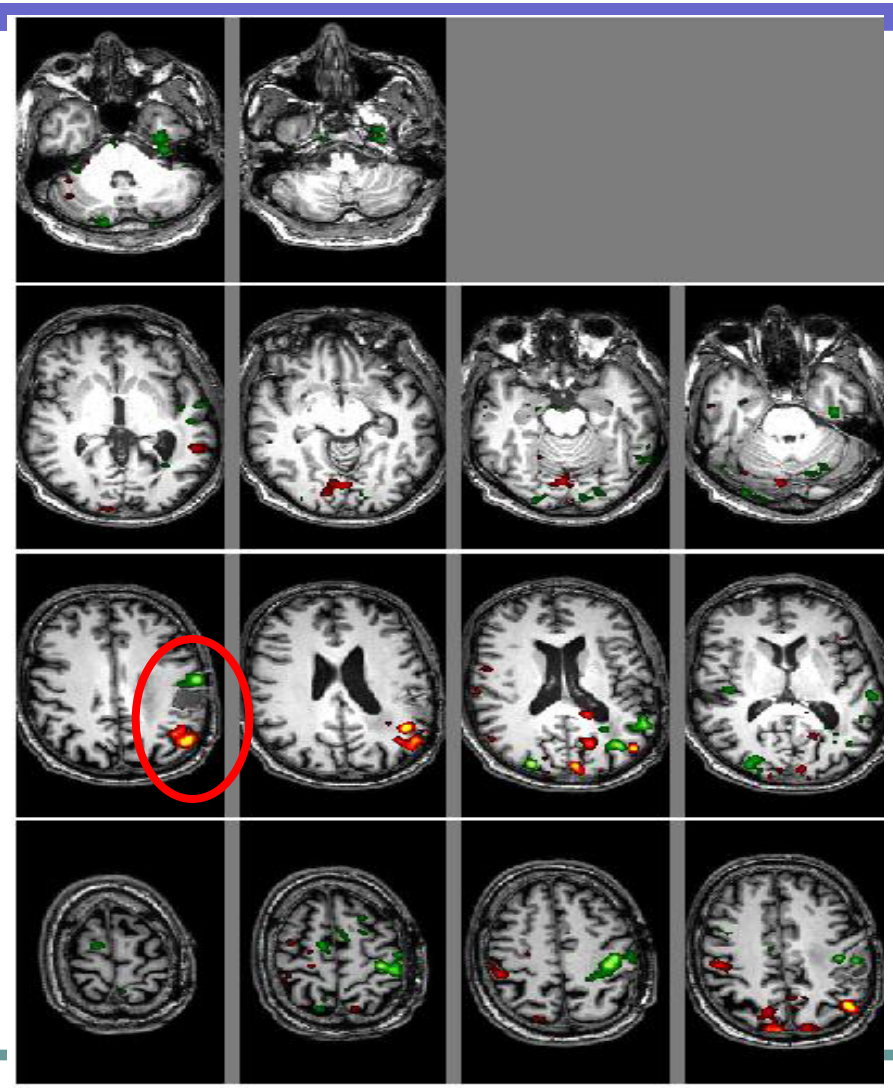




Engel 1a MEG CSI results
Difference Connectivity rest state run2

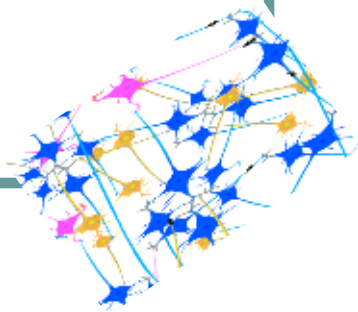


(Out > In):RED
(In > Out):Green

2.55
2.28
2.01
1.74
1.48

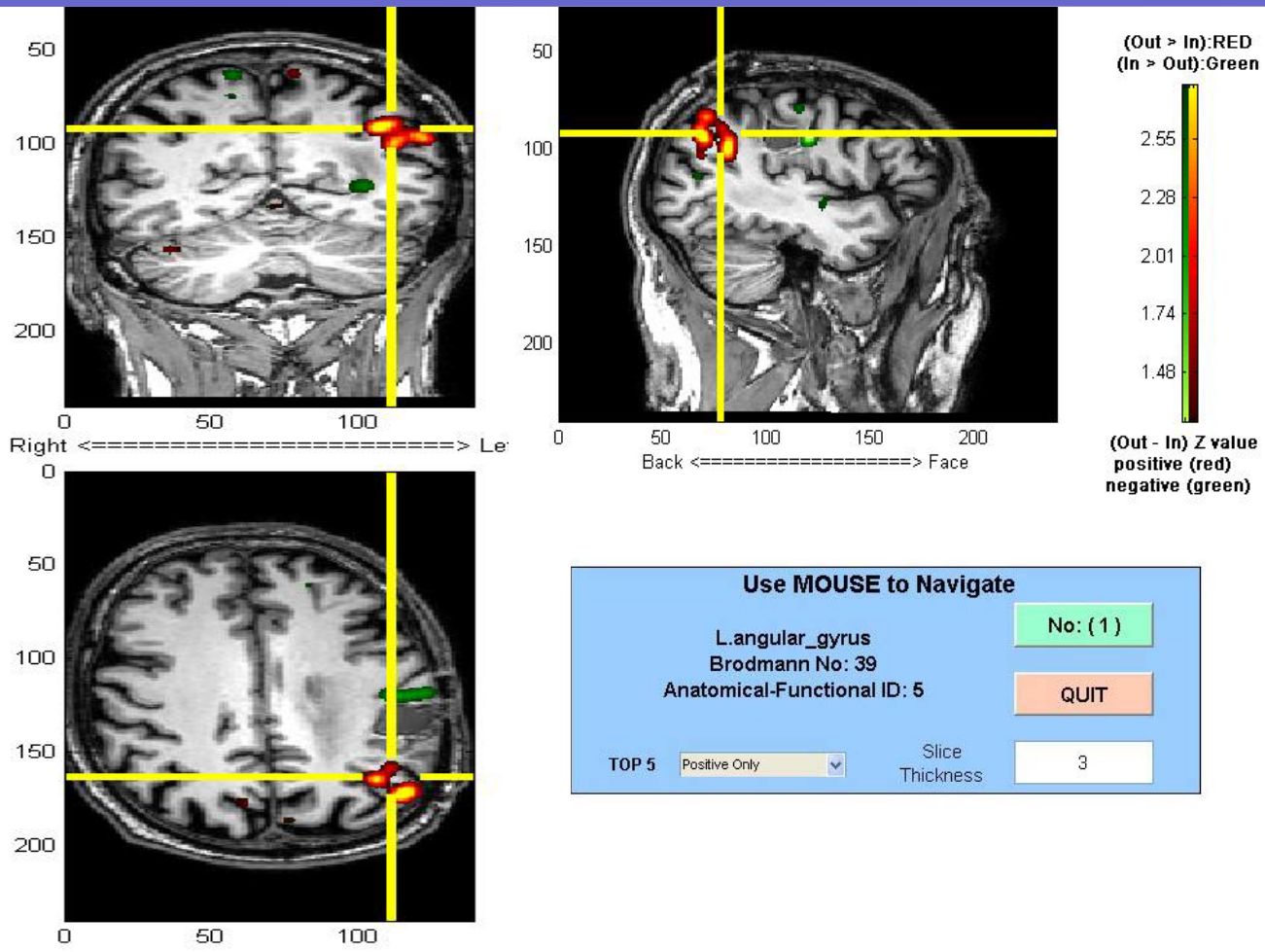
(Out - In) Z value
positive (red)
negative (green)

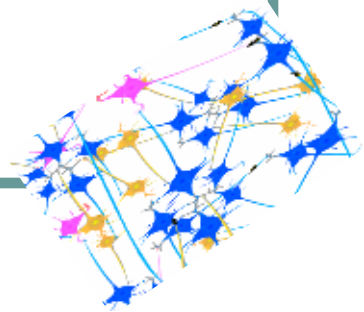
Right <----------> Left



Engel 1a MEG CSI results

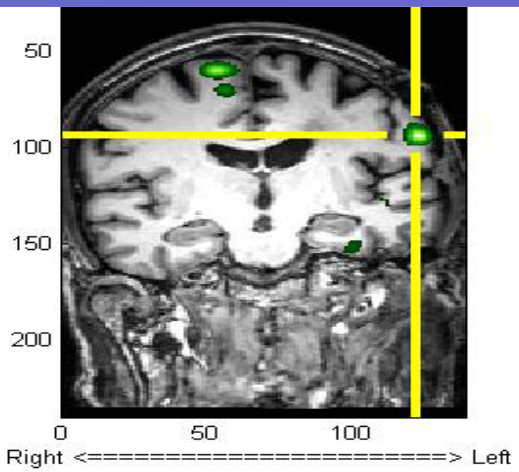
Difference Connectivity rest state run2—Top sender

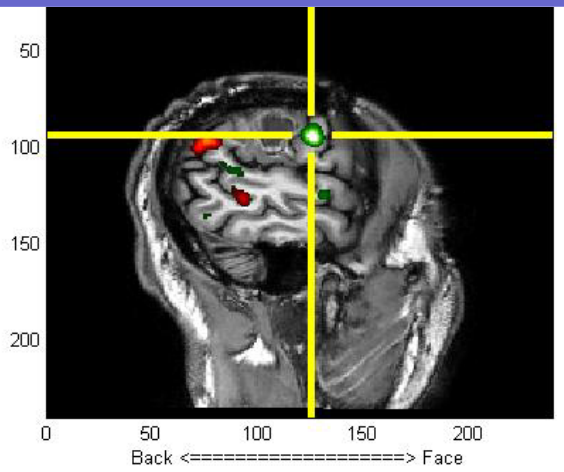


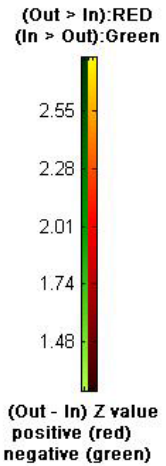


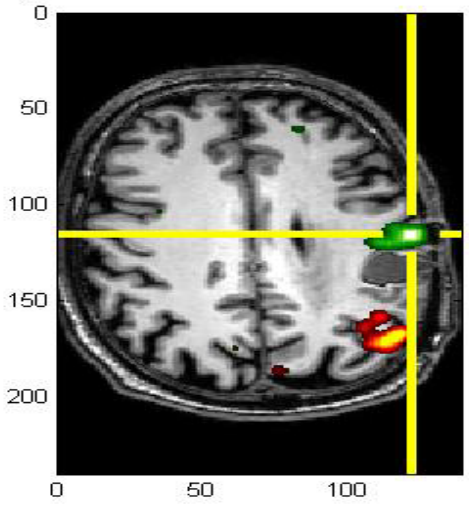
Engel 1a MEG CSI results

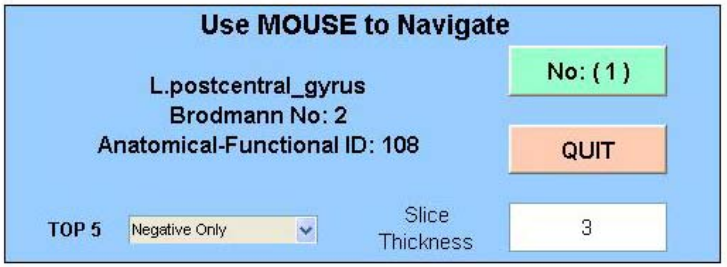
Difference Connectivity rest state run2—Top Receiver

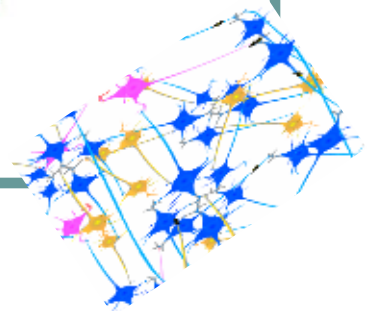






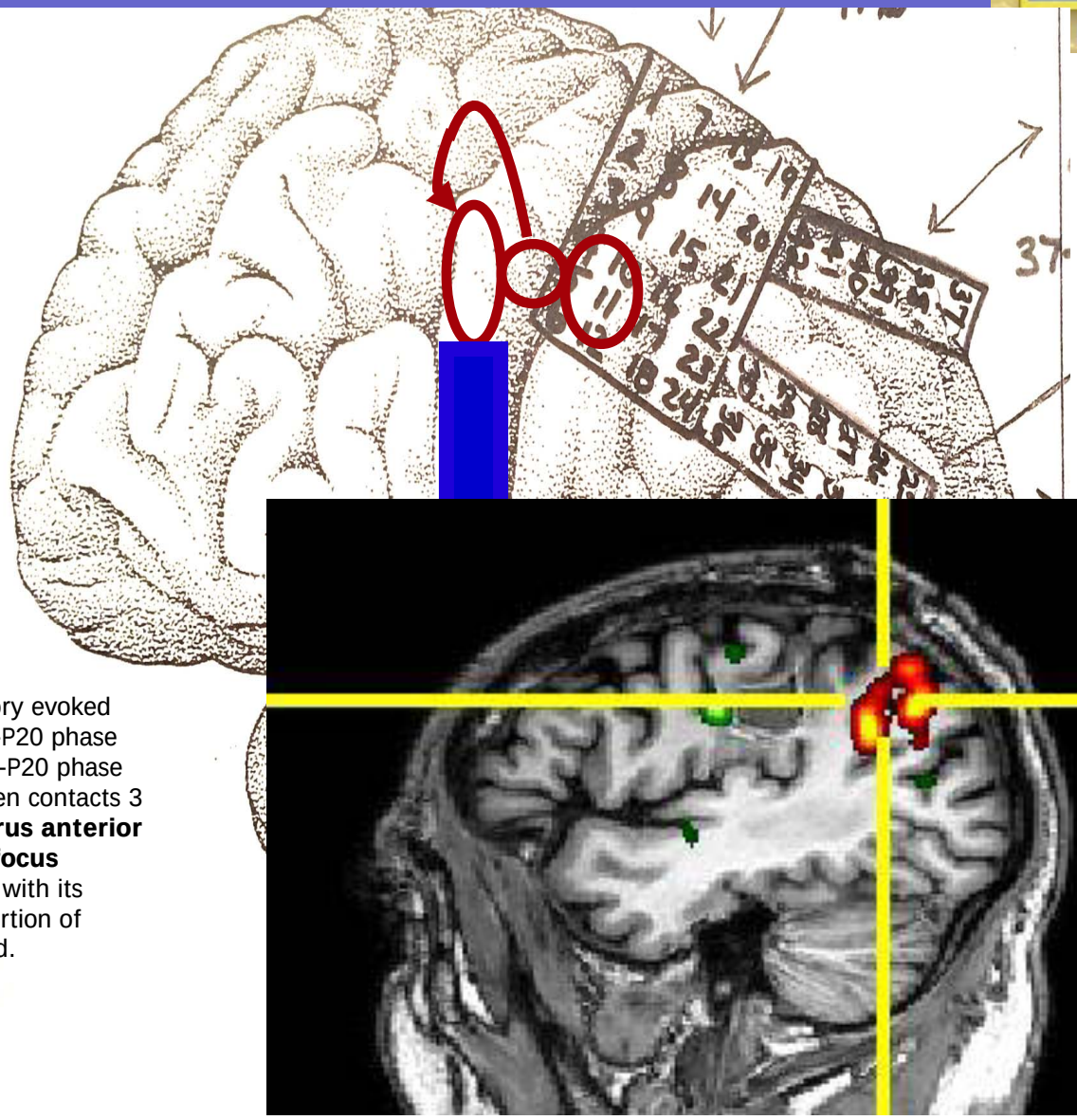






Engel 1a IEEG Results

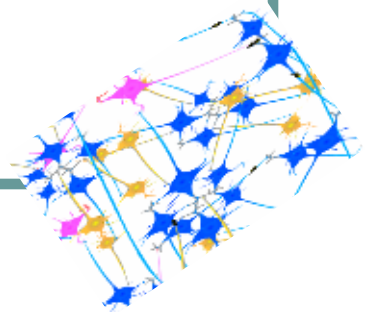
The **areas of the most seizure activity (contact 11) and initial spread (5, 6, 12, 17 and 18)** were marked with a cut number. The perirolandic grid was removed. A new 4 contact strip was placed over the cortex perpendicular to the central sulcus. SSEPs were used to localize the central sulcus with N20-P20 phase reversal. **The postcentral gyrus was localized anteriorly, with its posterior portion under the anterior portion of contacts 5 and 6, indicating that the epileptogenic zone was safe to resect.**



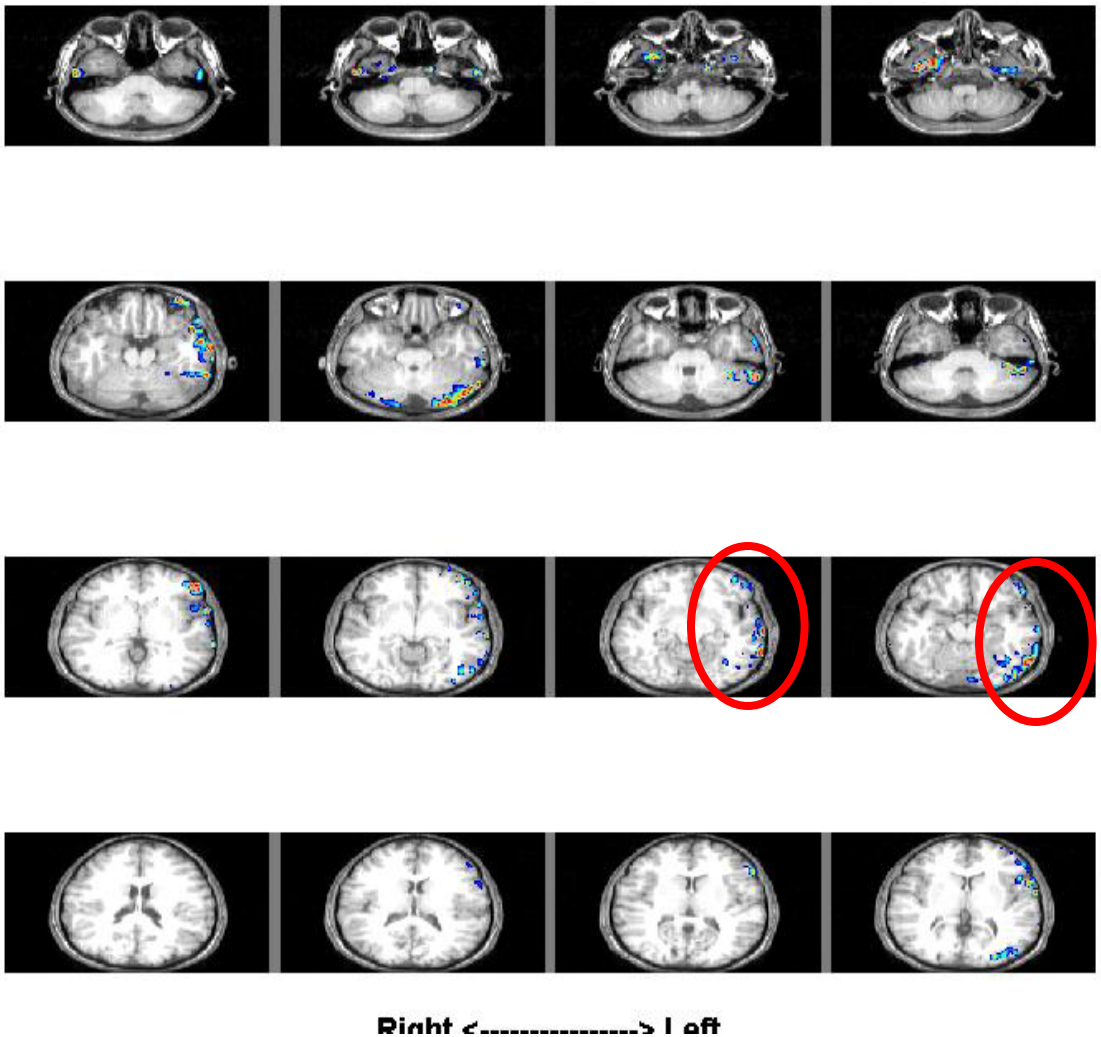
Consistently reproducible somatosensory evoked responses were obtained and the N20-P20 phase reversal was easily identified. The N20-P20 phase reversal consistently took place between contacts 3 and 4, **localizing the postcental gyrus anterior to the site of the primary seizure focus (contact #5 of the subdural grid),** with its posterior portion under the anterior portion of contacts # 5 and 6 of the subdural grid.

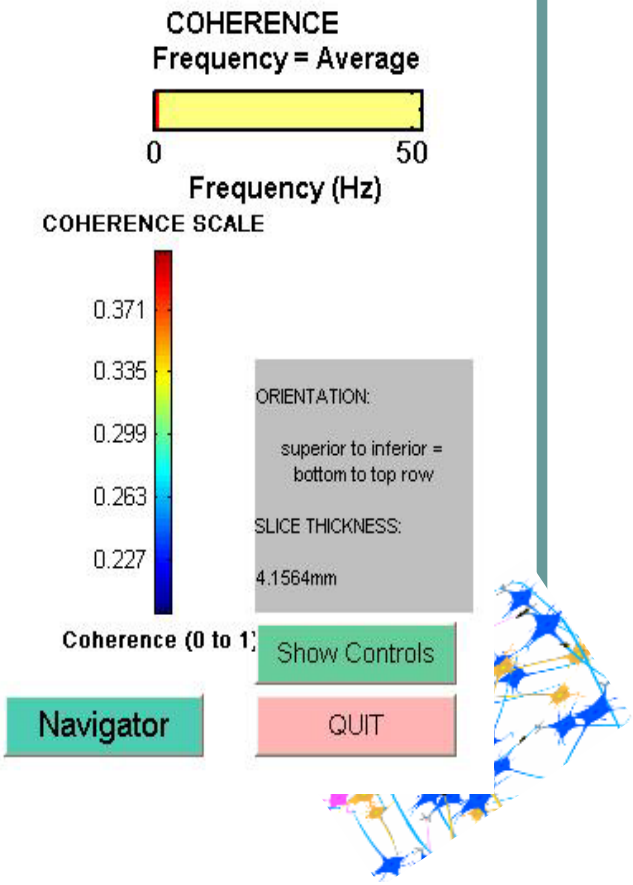
Engel 2 outcome

- 2842 ZA
- COH sending and receiving ablated was doing well.
- Location of Visualase treatment (thermal laser ablation)- Left inferior temporal gyrus
- Engle outcome - 1a now a 2
- ILEA outcome - 1 now a 2

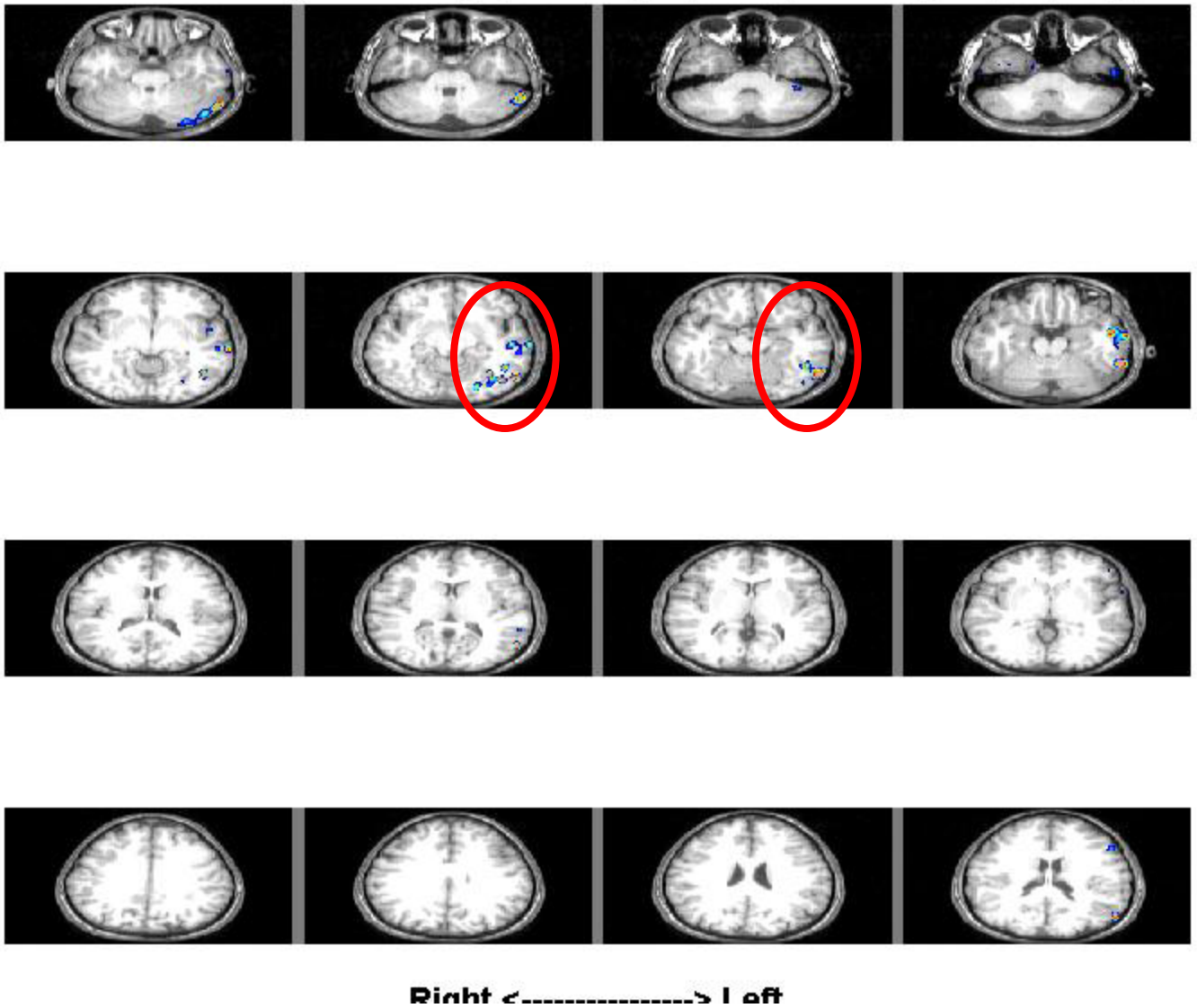


Engel 2 MEG CSI results
Coherence rest state run1



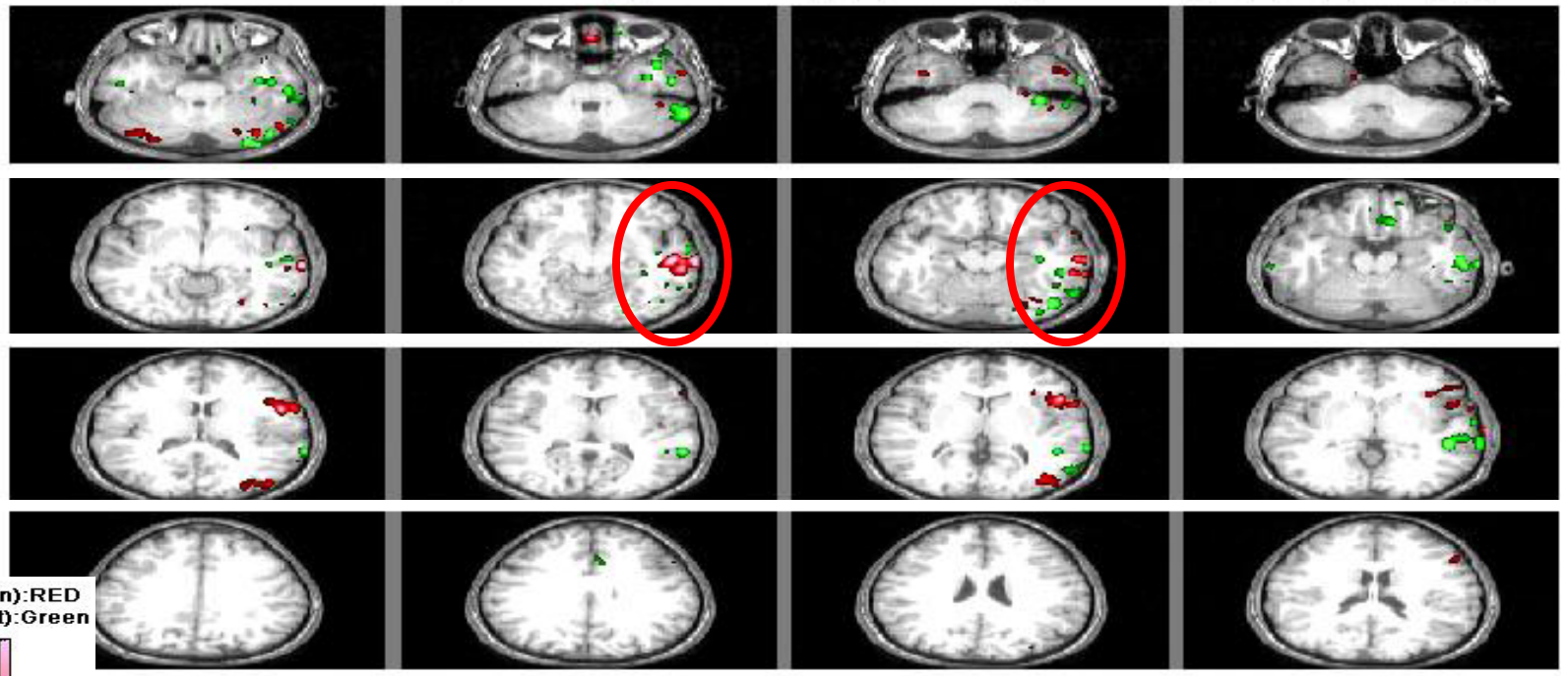


Engel 2 MEG CSI results
Persistence rest state run1



Engel 2 MEG CSI results

Difference Connectivity rest state run1

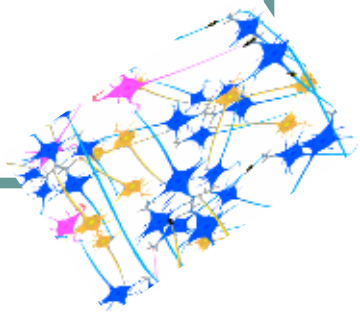


(Out > In):RED
(In > Out):Green

3.17
2.91
2.65
2.39
2.13

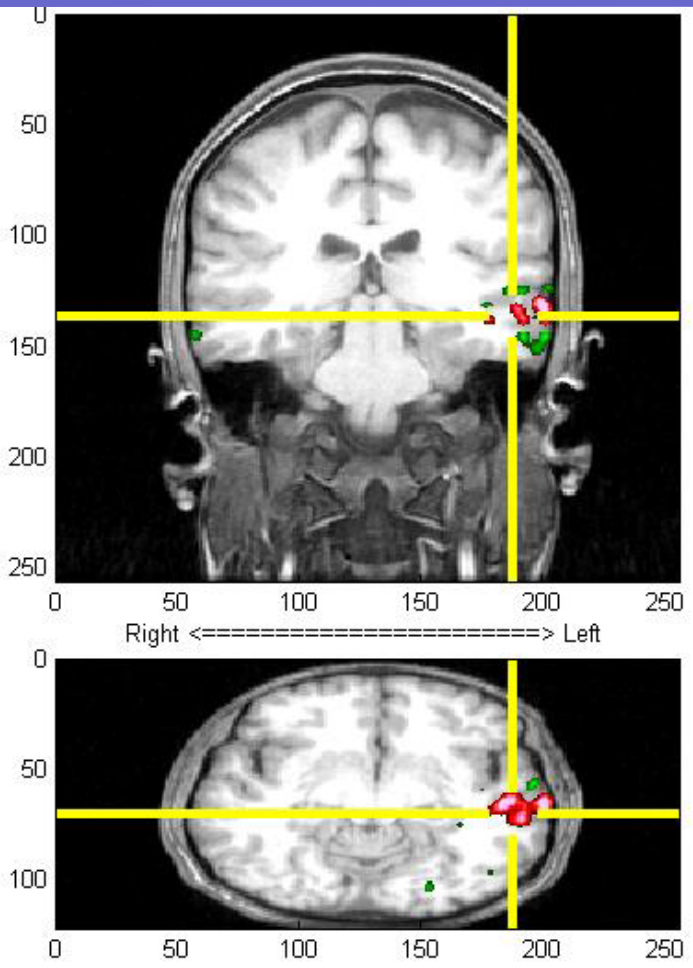
(Out - In) Z value
positive (red)
negative (green)

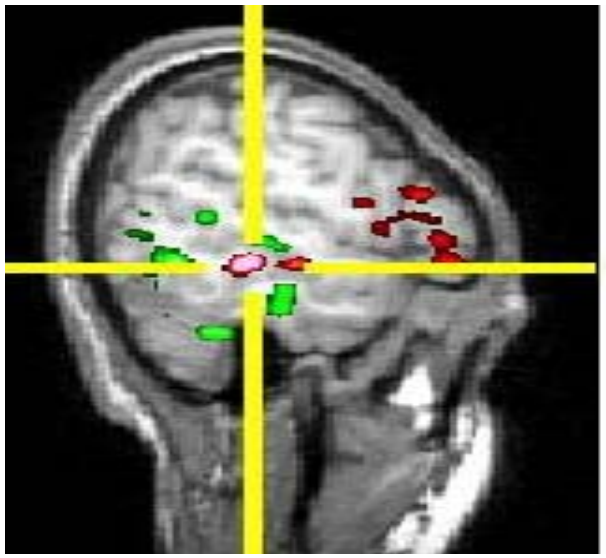
Right <----------> Left

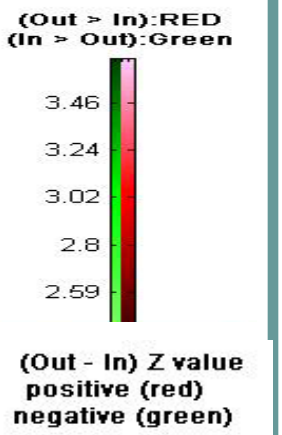


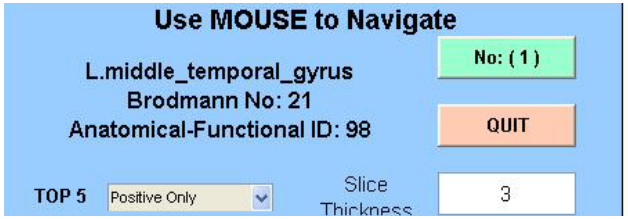
Engel 2 MEG CSI results

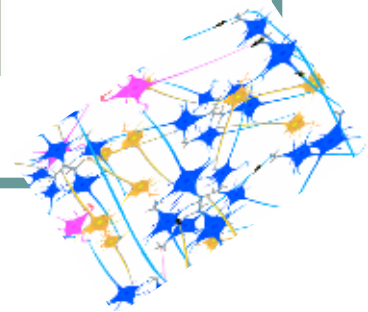
Difference Connectivity rest state run1—Top sender





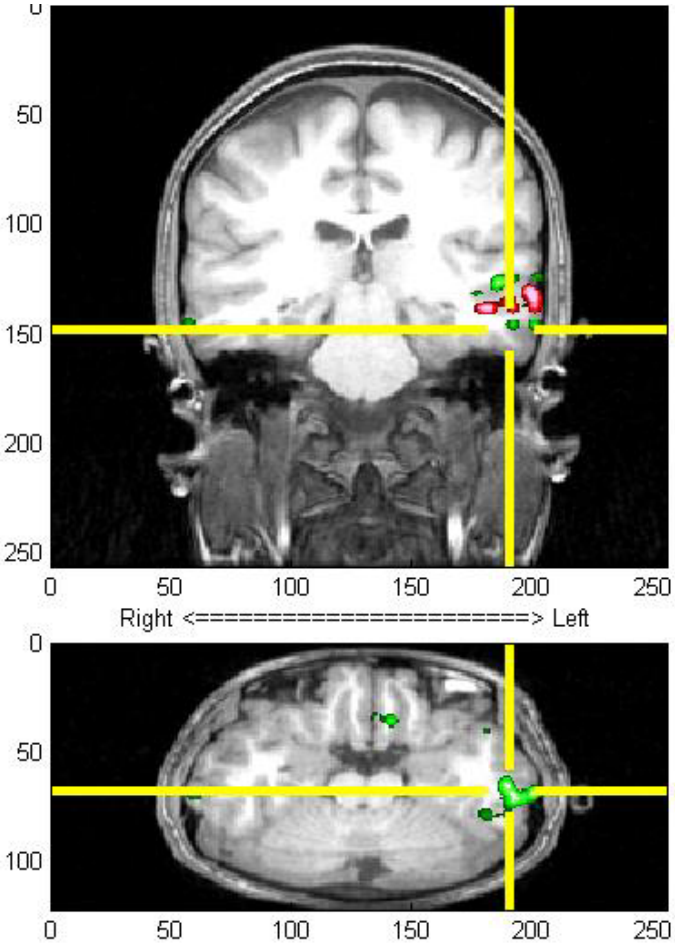


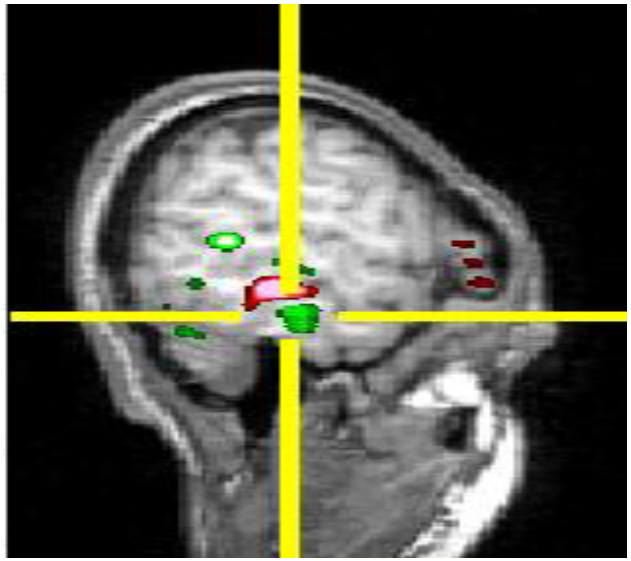


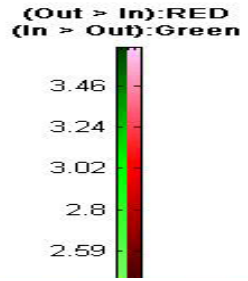


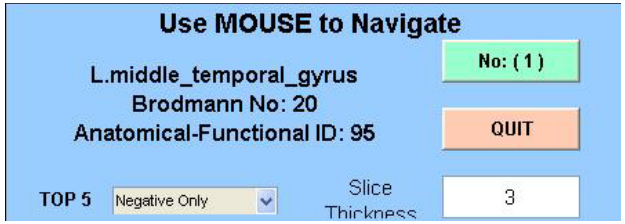
Engel 2 MEG CSI results

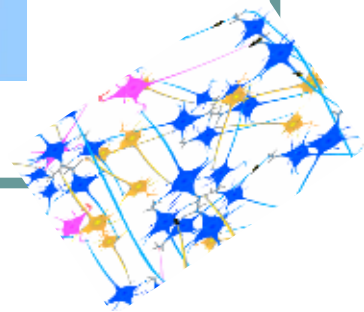
Difference Connectivity rest state run1—Top Receiver











Engel 2 SEEG

Coverage

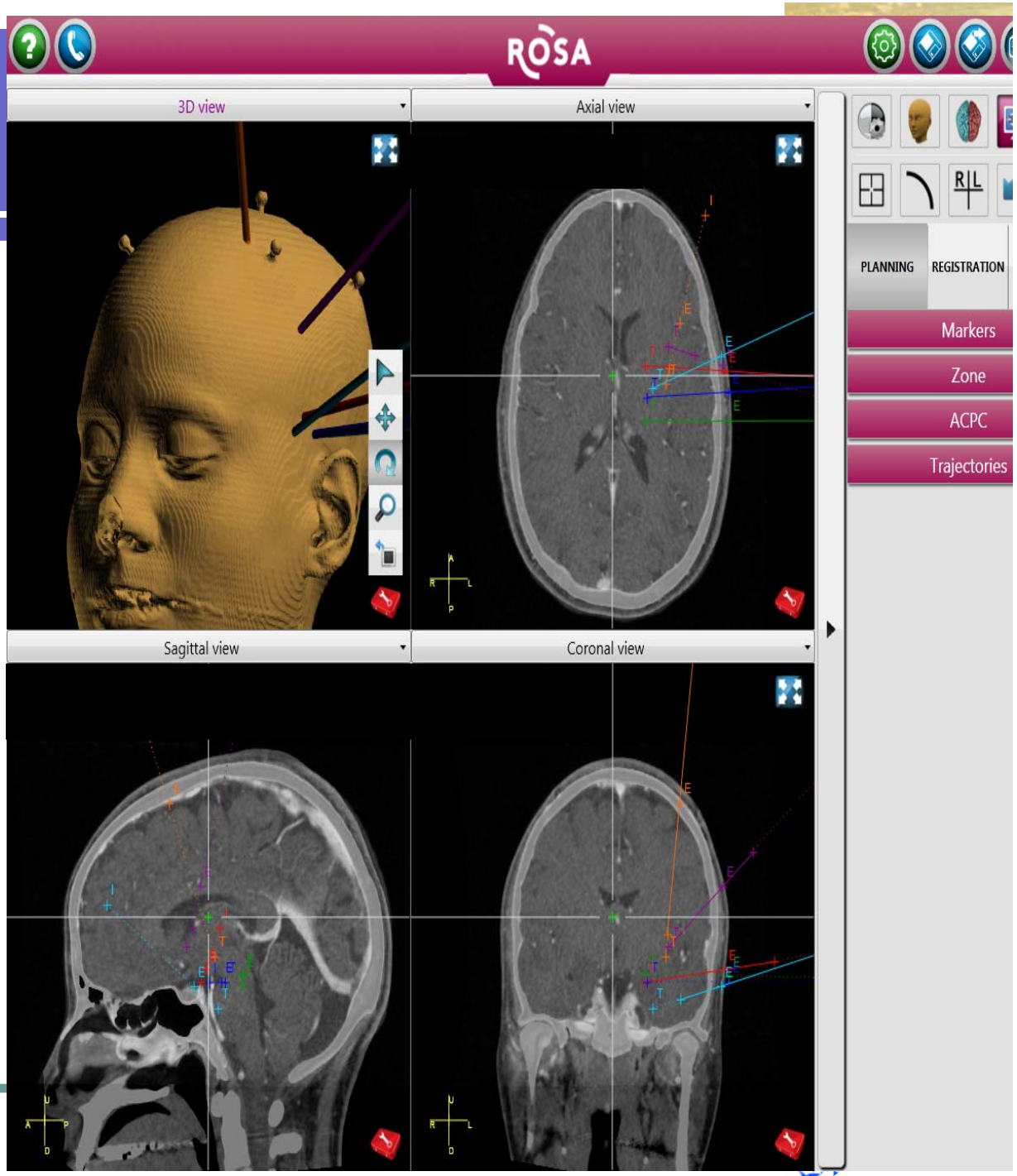
A’ - Anterior hippocampus/amygdala

B’ - Mid-hippocampus

C’ - Posterior hippocampus

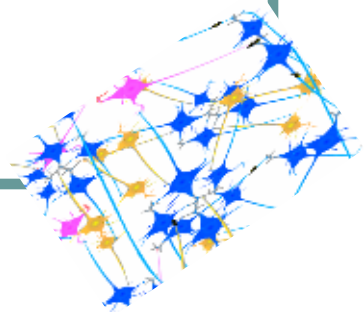
D’ - Transfrontal anterior insula

E’ - Lateral oblique posterior insula

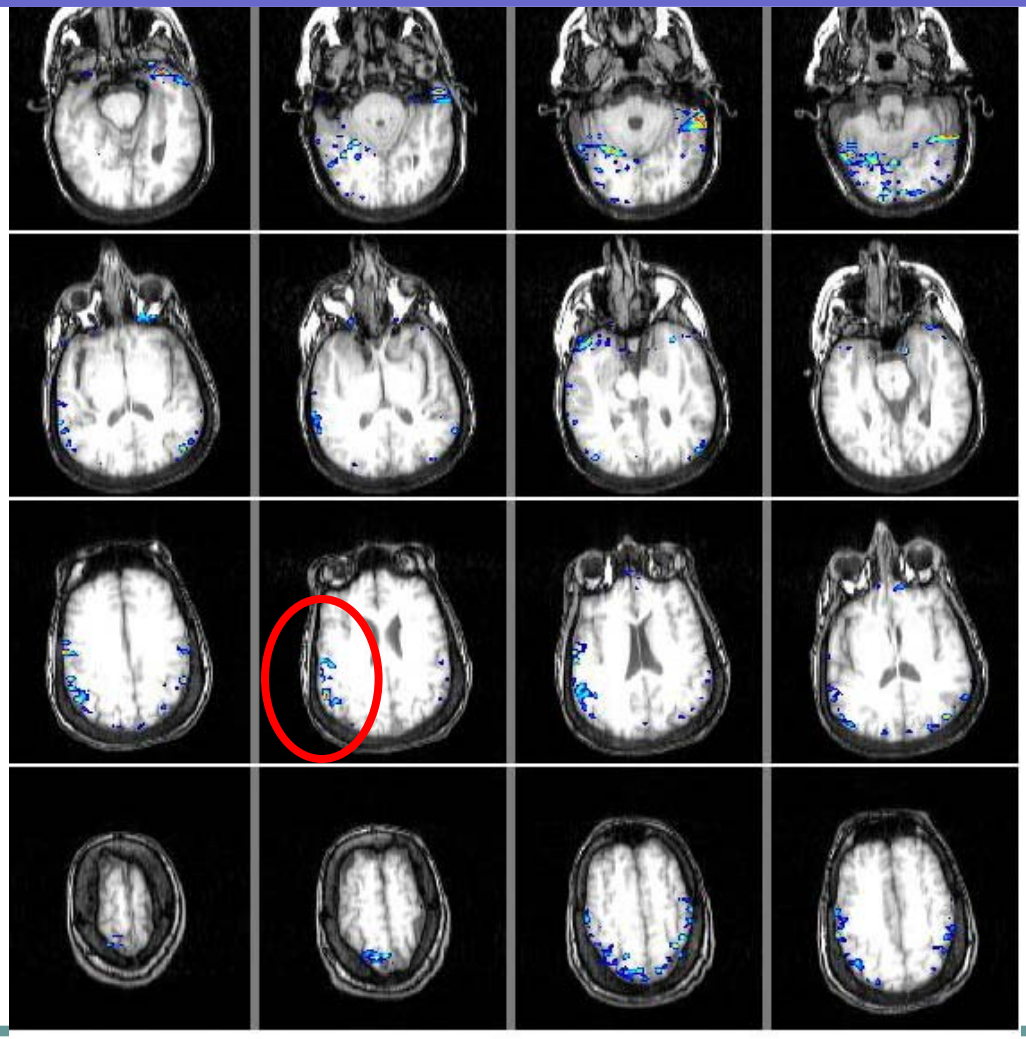


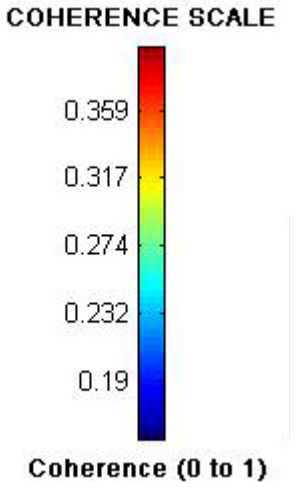
Engel 4b outcome

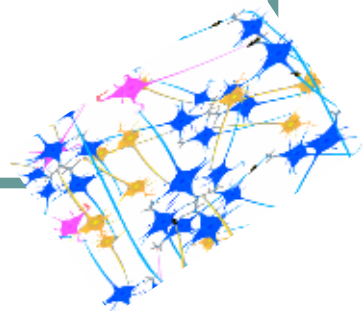
- 2637 LO
- COH sending removed and doing poor.
- Location of resection- Right temporal lobe
- Engle outcome - 4b
- ILEA outcome - 5



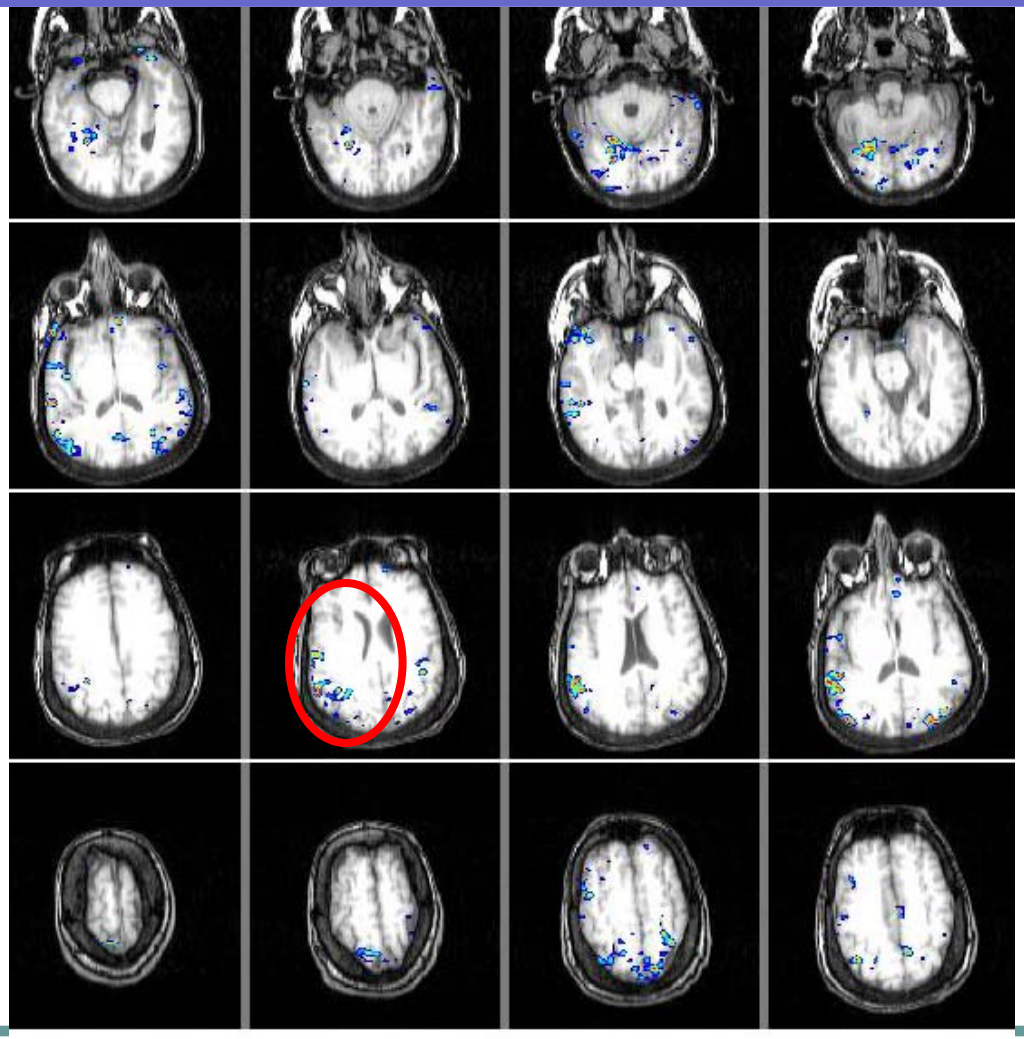
Engel 4b MEG CSI results
Coherence rest state run4

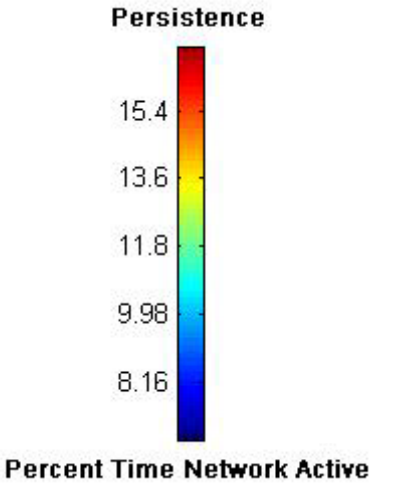


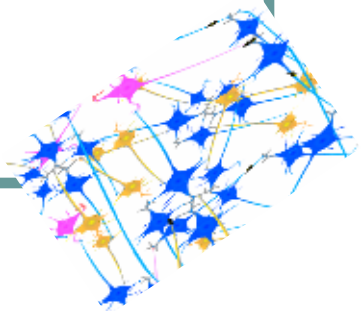




Engel 4b MEG CSI results
Persistence rest state run4



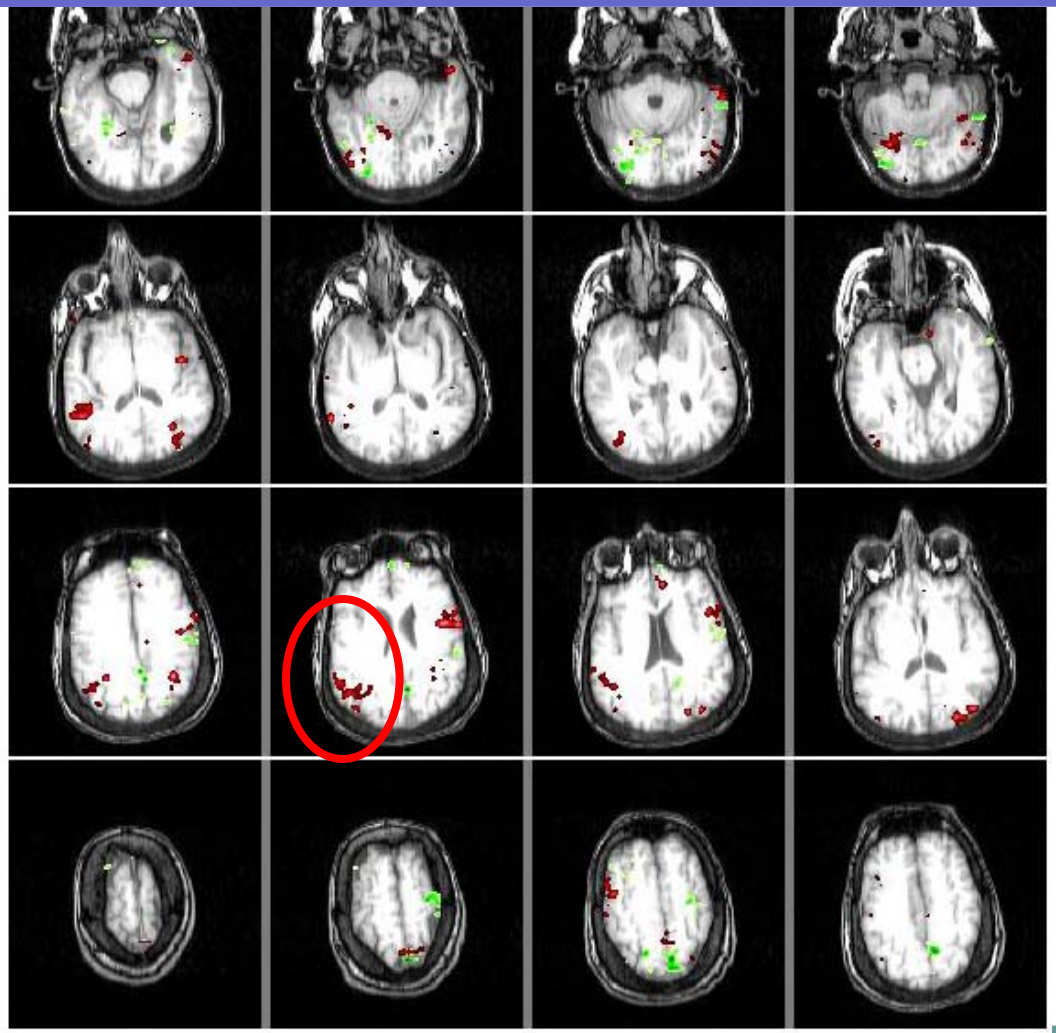




Right <----------> Left

Engel 4b MEG CSI results

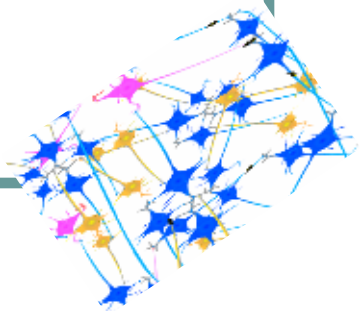
Difference Connectivity rest state run4



(Out > In):RED
(In > Out):Green

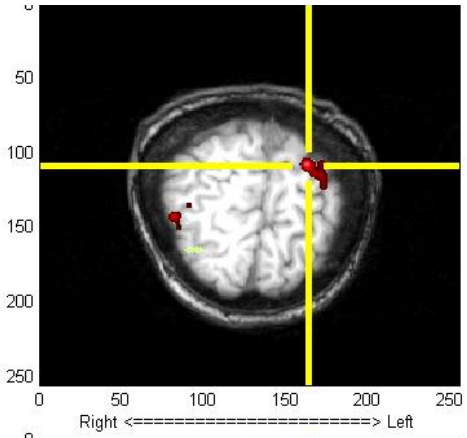
2.37
2.12
1.87
1.62
1.37

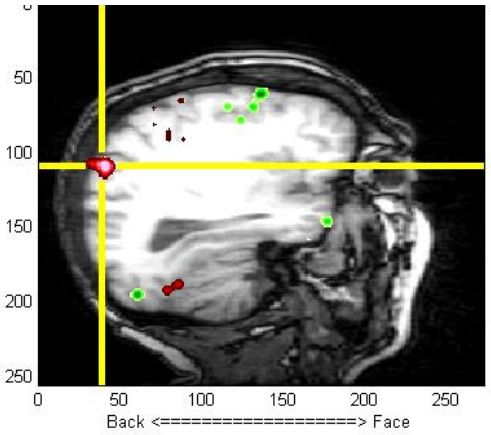
(Out - In) Z value
positive (red)
negative (green)

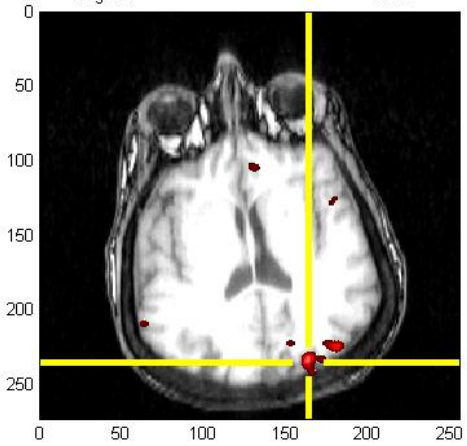


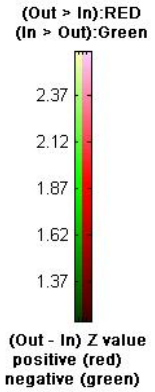
Engel 4b MEG CSI results

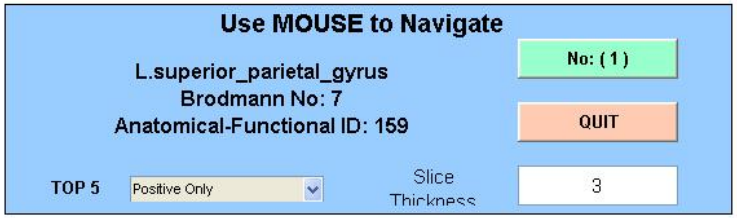
Difference Connectivity rest state run1—Top sender

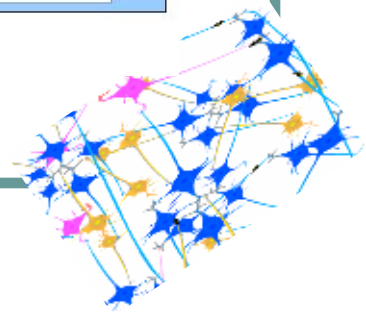












Engel 4b MEG CSI results

Difference Connectivity rest state run1—Top Receiver

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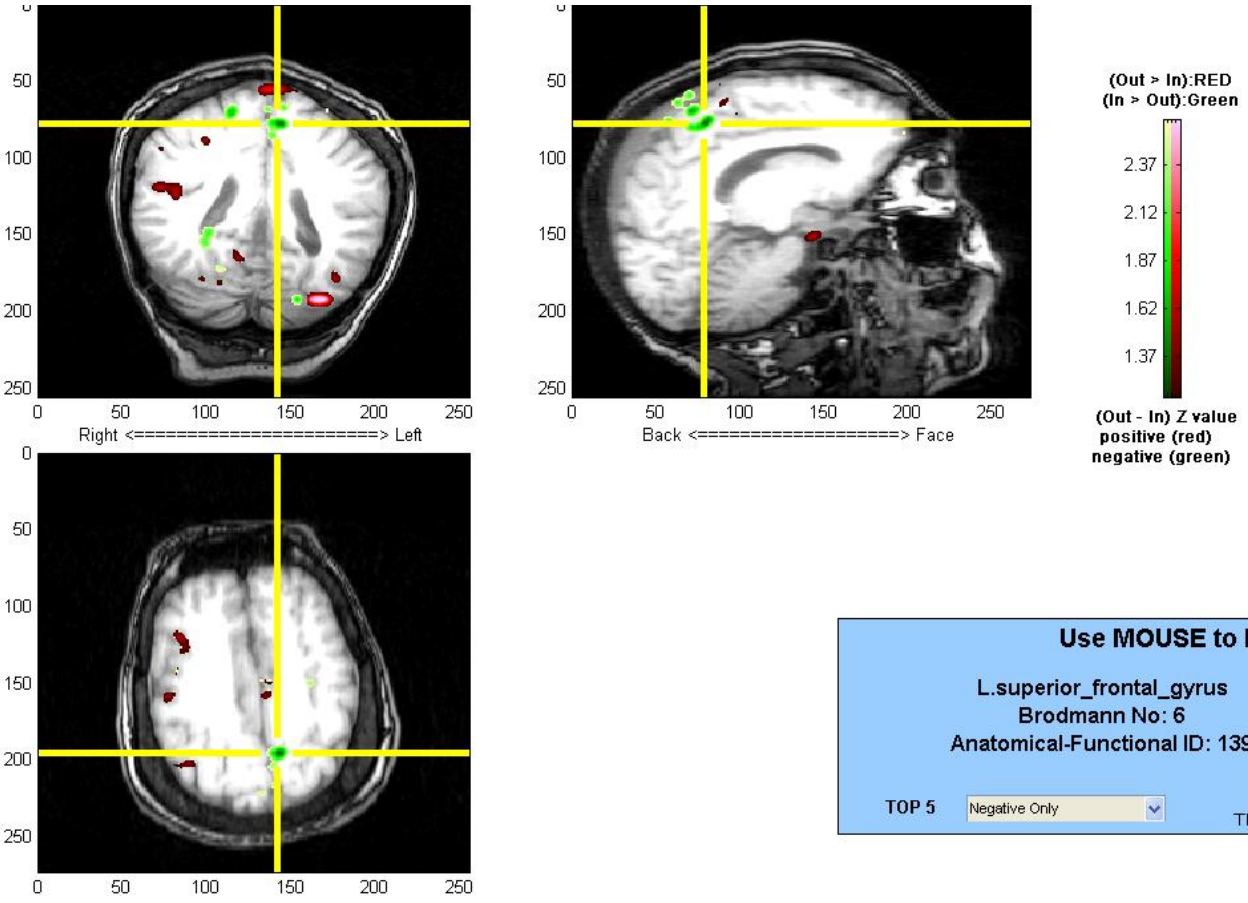
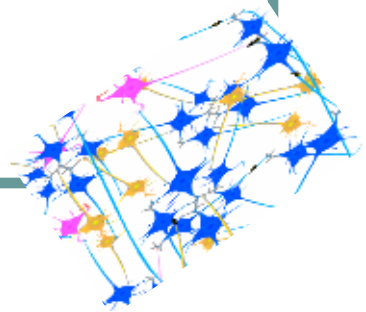
Halifax



Conclusions

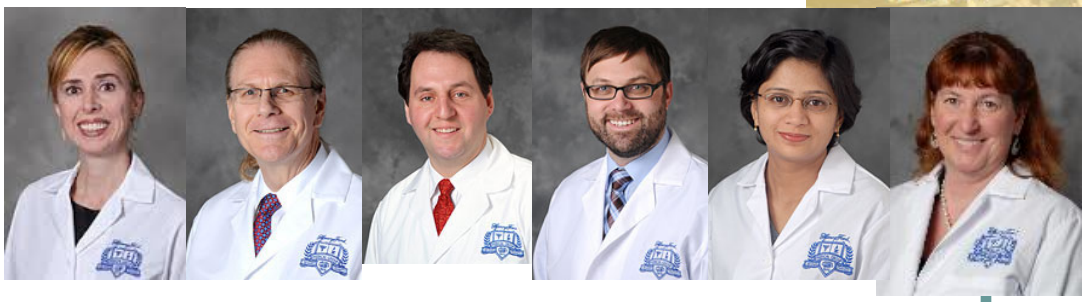
- We used MEG to determine the network properties in patients with epilepsy to identify the flow of information in the epileptic network.
- The MEG results from coherence source imaging (CSI) can provide information on the location of brain regions that are dominant and the direction and level of communication between brain regions.
- Our study found that resection of high coherent areas that were receivers as opposed to a sender appeared to result in a worse outcome.
- This may be due to the nature of a receiving area in the brain being the regions where the epilepsy propagated to, as opposed to the location where the epilepsy initiated.
- We hypothesize that the epileptic network is very dynamic and highly plastic and therefore may be able to change the direction of information flow.



Thank you for your attention!

Thank You to Our Collaborators:

Gregory L. Barkley, MD
Karen M Mason, REEG/MEG Tech
Jason Schwalb, MD
Basel Assaad, MD
Jules Constantinou, MD
Shailaja Gaddam, MD
Naznin Mahmood, MD
Robert Simkins, MD
Marianna Spanaki-Varelas, MD
Vibhangini Wasade, MD
John E Moran, PhD
Steven Robinson PhD
Valentina Gumenyuk, PhD
Barbara Weiland PhD
Kost Elisevich, MD, PhD
Brien J. Smith MD
Norman Tepley, PhD



Acknowledgement

Research supported by
NIH/NINDS
Grant RO1-NS30914