Conference on Systems Neuroscience
and Rehabilitation: SNR2014
Saitama, Japan, March 2014

MEG source-space connectivity analysis

**Estimation and Visualization of Brain Networks
Using MEG Brain Imaging**

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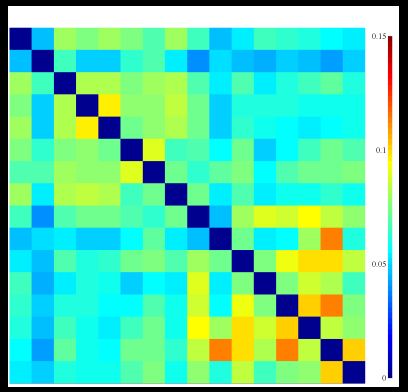
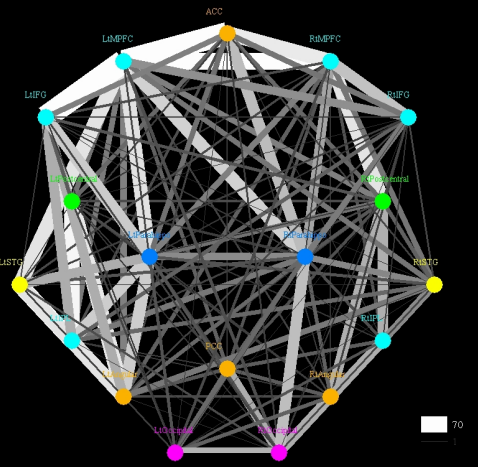
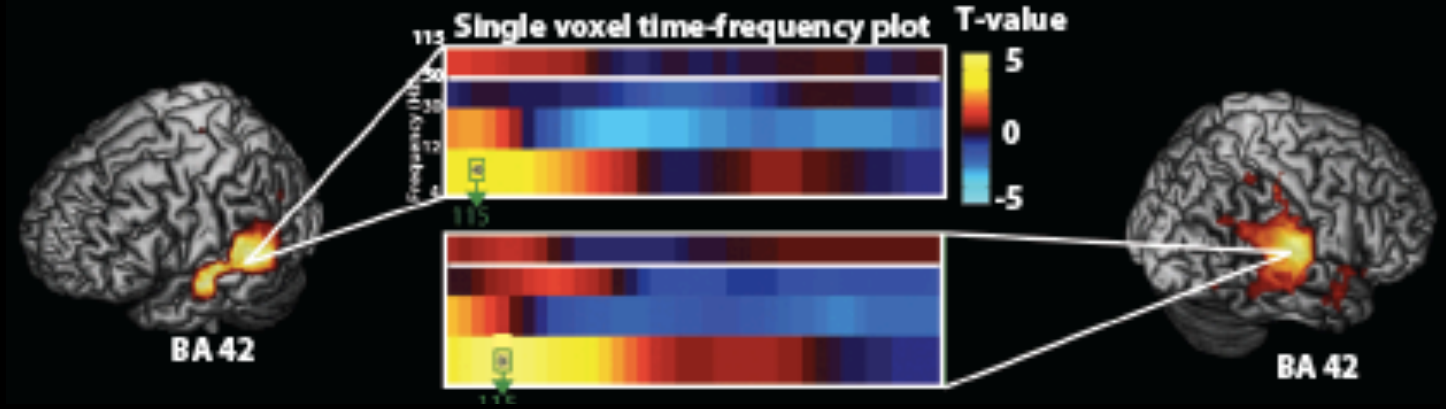
Powerful breakthroughs have occurred in imaging algorithms for biomagnetic brain imaging

Reconstructing functional connectivity networks





Reconstructing activation sequences with high temporal and frequency resolution



These advances open up new applications in basic and clinical neuroscience

Beamformer

Beamformer virtually manipulates the sensitivity profile of the sensor array to create a focused sensitivity region.

This focus is scanned throughout the entire brain region to provide three dimensional reconstruction.

Beamformer applies a location-dependent linear weight to the measured data.

$$\hat{s}(\boldsymbol{r},t) = \boldsymbol{w}^T(\boldsymbol{r})\boldsymbol{b}(t) = [w_1(\boldsymbol{r}),\ldots,w_M(\boldsymbol{r})]\begin{bmatrix} b_1(t) \\ \vdots \\ b_M(t) \end{bmatrix} = \sum_{m=1}^{M} w_m(r)b_m(t)$$

Narrow-band adaptive beamformer

Frequency-specific weight

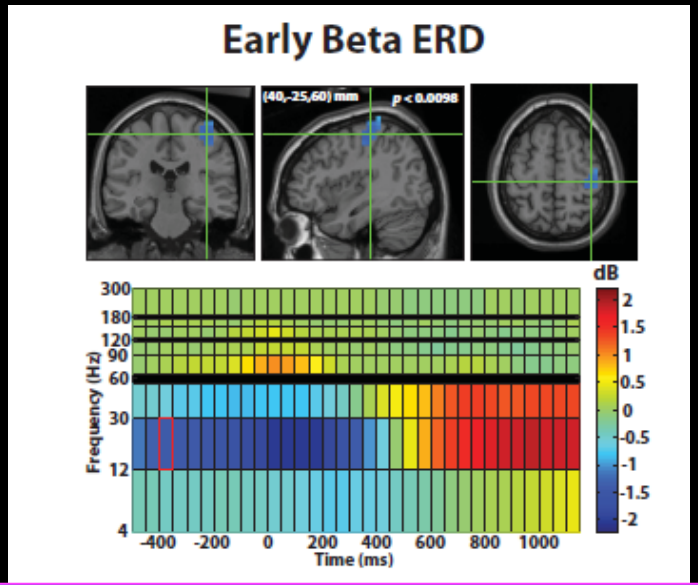
$\boldsymbol{R}(f)$: Covariance matrix calculated from the target frequency band of the signal.

$$\boldsymbol{w}(f) = \boldsymbol{R}(f)\,\boldsymbol{l}(\boldsymbol{r}) \,/\, [\boldsymbol{l}^T(\boldsymbol{r})\boldsymbol{R}(f)\,\boldsymbol{l}(\boldsymbol{r})]$$

The weight is tuned to a specific frequency band of brain rhythms of interest.

Example of 5D(space-time-frequency) imaging of hand-motor activation

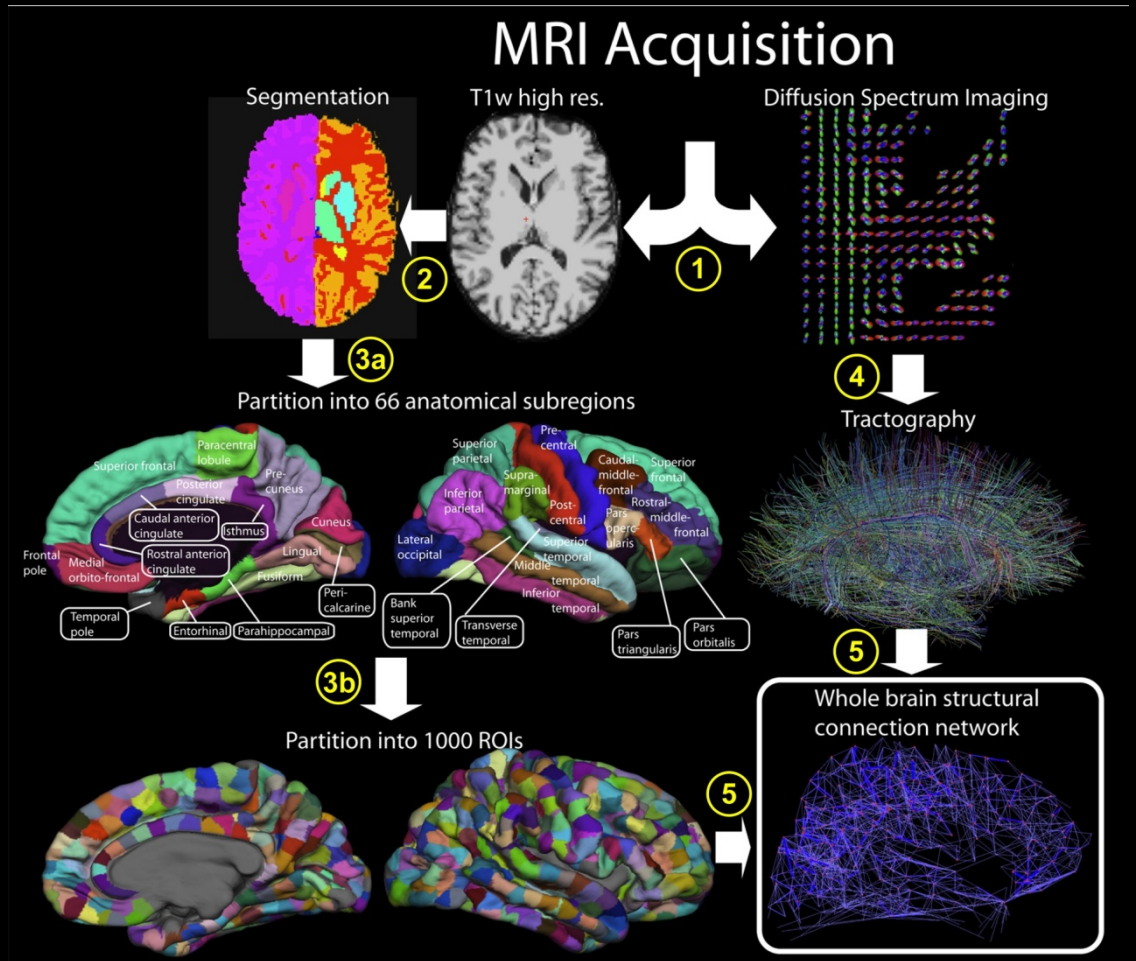
Voluntary right index finger movement.

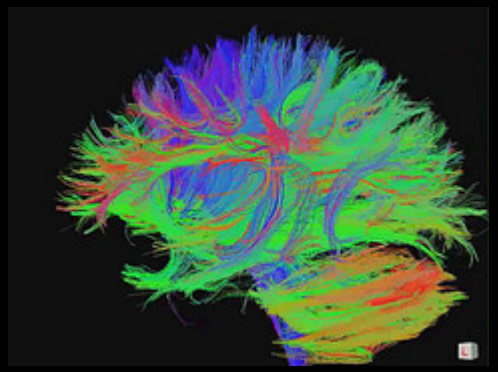


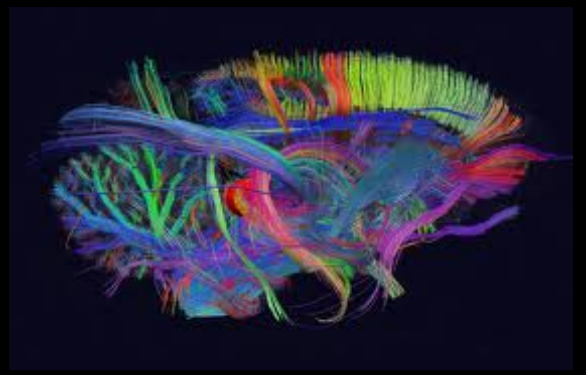
The time-frequency map of source activity is reconstructed at all voxel locations.

The frequency selective source imaging method is well suited to source-space functional connectivity analysis.

Anatomical connectivity vs. Functional connectivity

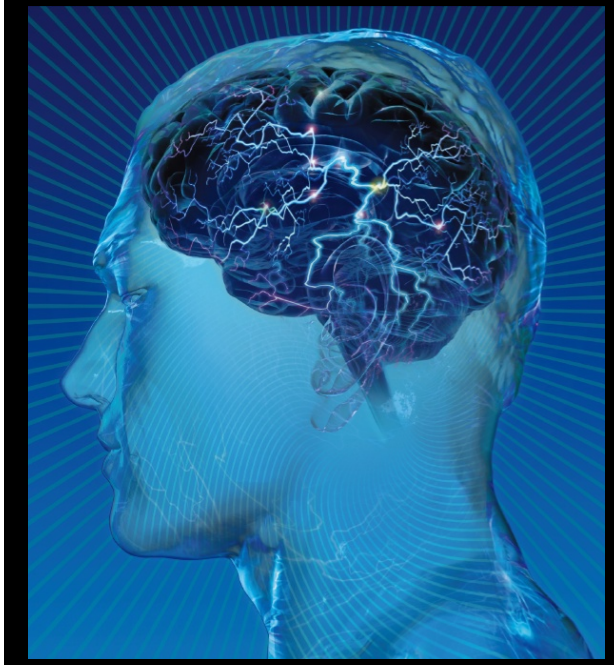






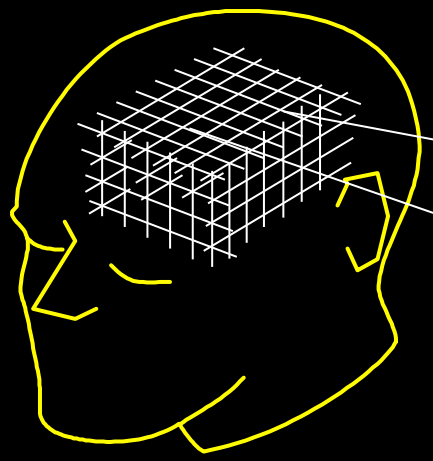
Anatomical (structural) network expresses the hardware wiring in a brain. Functional connectivity expresses whether communication is actually taken place through the hardware wiring.

Brain functional connectivity analysis using source space



- A growing number of investigations use the source space analysis.
- The source space analysis first estimates source activity using an inverse method, and computes connectivity metric using the estimated source activities.
- A most popular metric is coherence.

Voxel pair-wise coherence metric



voxel time courses **voxel spectra**

$$s_k(t) \longrightarrow \sigma_k(f) = \int s_k(t) e^{-2\pi i f t} dt$$

$$s_j(t) \longrightarrow \sigma_j(f) = \int s_j(t) e^{-2\pi i f t} dt$$

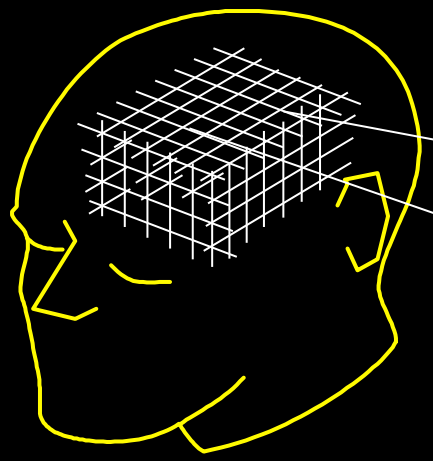
The average is computed using epoch/trial averaging

$$\eta_{k,j}(f) = \left| \frac{\langle \sigma_k(f) \sigma_j(f)^* \rangle}{\sqrt{\langle |\sigma_k(f)|^2 \rangle \langle |\sigma_j(f)|^2 \rangle}} \right|$$

Seed coherence:

- When computing voxel coherence, a reference voxel is first determined, and coherence map is computed between this reference voxel, called the seed voxel, and all other voxels.
- We can further scan the seed voxel to obtain all-voxel-to-all-voxel coherence matrix.

Voxel pair-wise coherence metric



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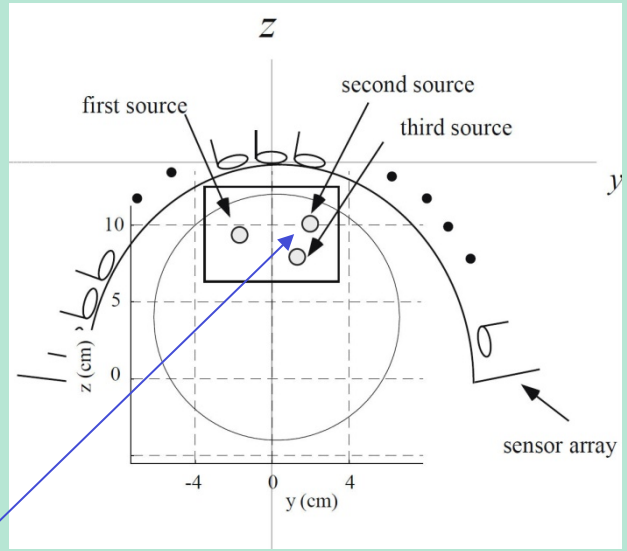
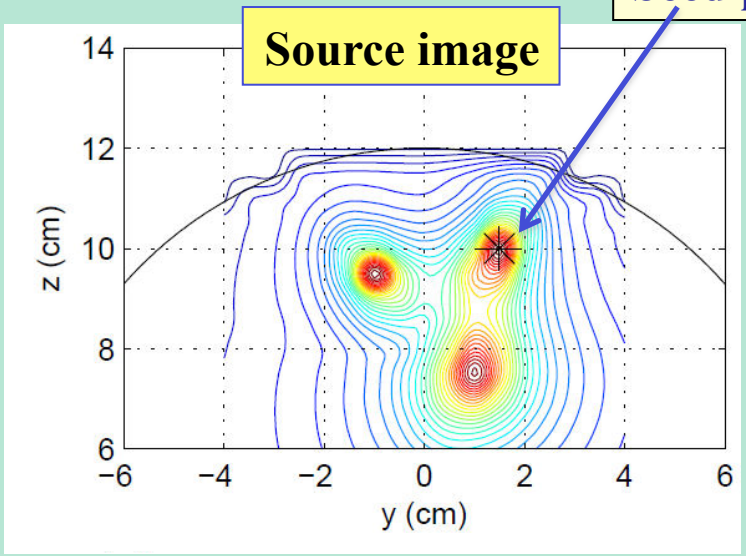
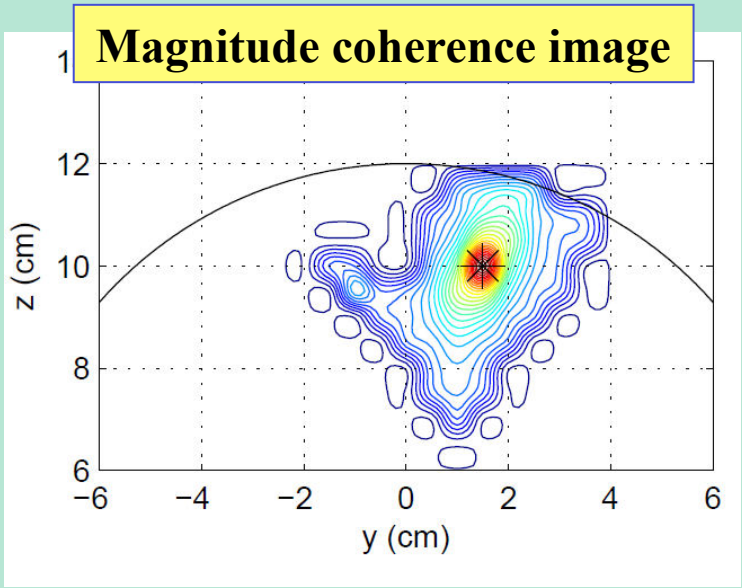
Seed blur – computer simulation



The second source interacts with the other two sources.





Magnitude coherence image only shows spurious peak caused by the leakage(blur) of imaging algorithm; the peak is referred to as the seed blur.

Imaginary part of coherence

In MEG source-space coherence analysis, we had better use the imaginary coherence to reduce spurious coherence caused due to algorithm leakage.

Why ??

Nolte et al. Clinical Neurophysiology, Vol.115, 2004
Sekihara, et al., IEEE Transactions on Biomedical Engineering , Vol.58, 2011

Imaginary part of coherence

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Coherence between the jth and kth voxels:

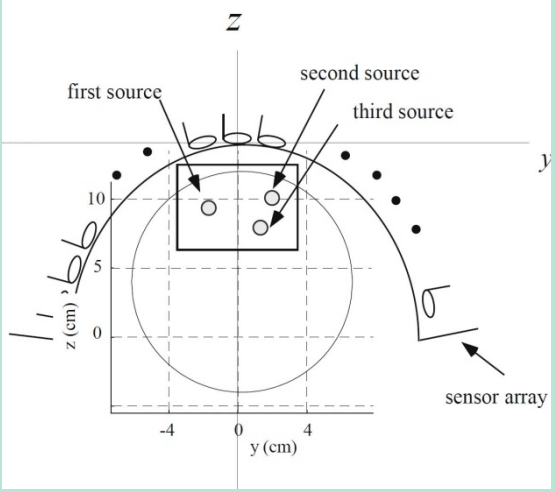
$$\eta_{j,k}(f) = \Re\left[\eta_{j,k}(f)\right] + i\Im\left[\eta_{j,k}(f)\right]$$

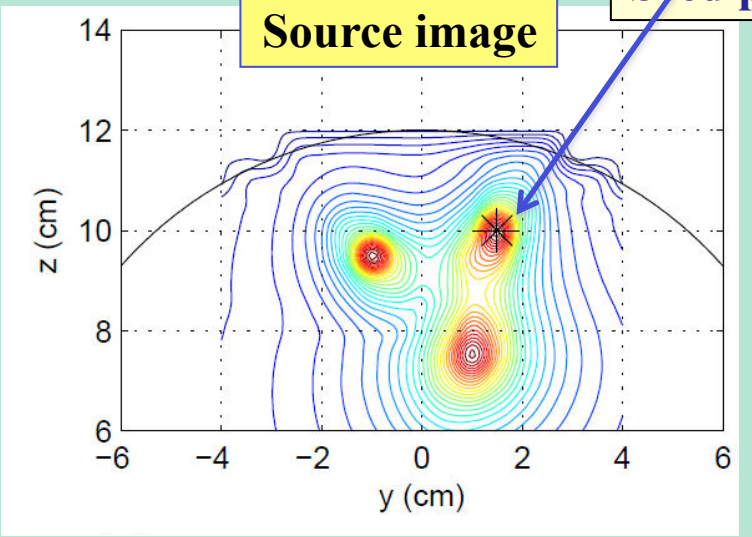
Real part:
- Corresponds to zero time-lag correlation.
- Can be caused from common interference sources.

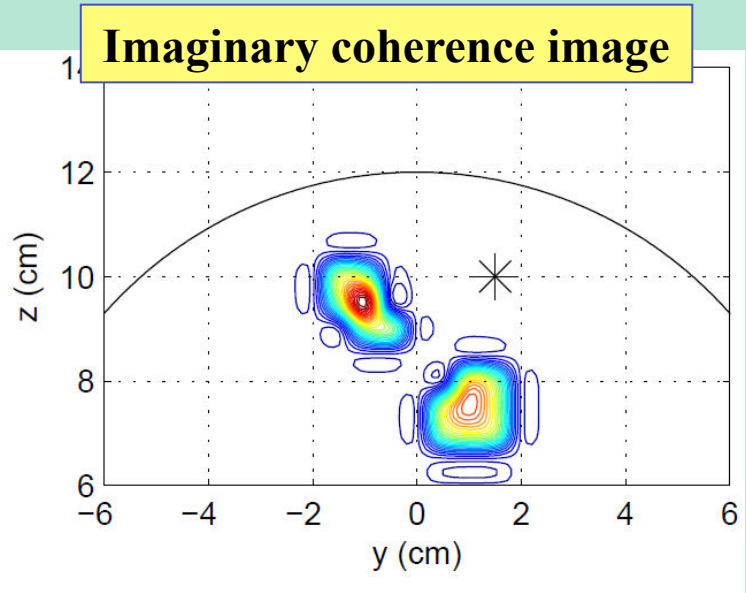
Imaginary part:
- Corresponds to non-zero time-lag correlation.
- Caused only by true brain interaction.

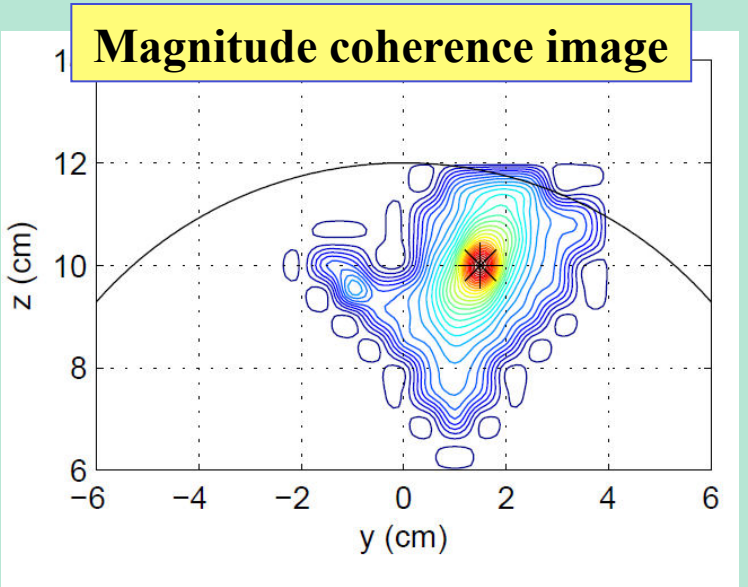
Nolte et al. Clinical Neurophysiology, Vol.115, 2004
Sekihara, et al., IEEE Transactions on Biomedical Engineering , Vol.58, 2011

Imaginary coherence– computer simulation



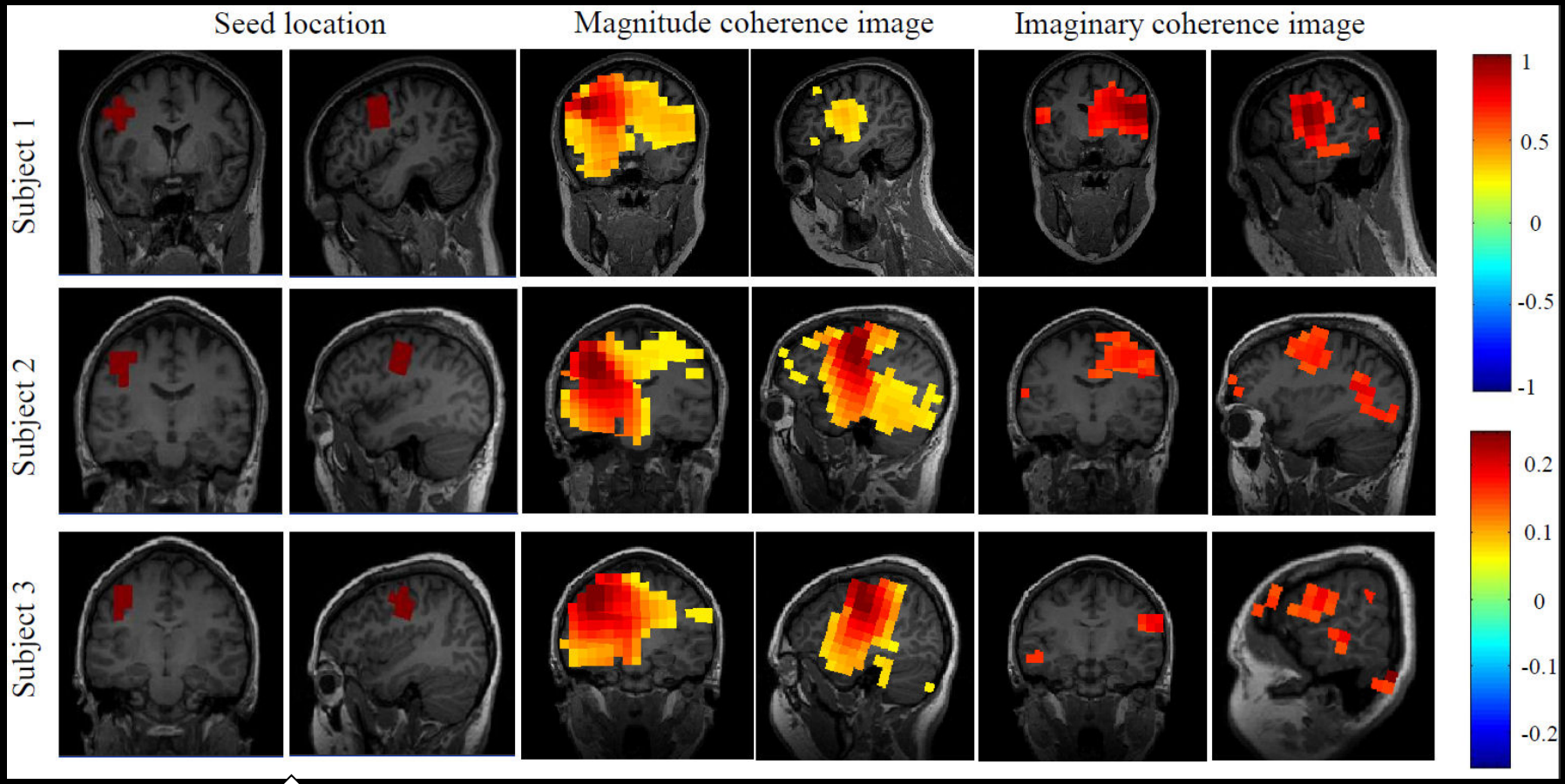






Imaginary coherence image does not contain the seed blur, and shows the two sources that are truly interacting with the seed source.

Seed blur:Resting-state MEG, beta-band coherence image



Voxels within the left pre-central gyrus (left primary motor area) were selected as seed voxels.

Mapping of mean imaginary coherence (MIC)

Coherence between the jth and kth voxels:

$$\eta(f, \mathbf{r}_j, \mathbf{r}_k) = \alpha(f, \mathbf{r}_j, \mathbf{r}_k) + i\beta(f, \mathbf{r}_j, \mathbf{r}_k)$$

Mean imaginary coherence for the jth voxel:

$$\bar{\beta}(f, \mathbf{r}_j) = \frac{1}{K} \sum_{k=1}^{K} | \beta(f, \mathbf{r}_j, \mathbf{r}_k) |$$

Magnitude of imaginary coherence is averaged over all voxel connections.

What does MIC mean ??

A. G. Guggisberg *et al.*, Annals of Neurology, Sep 25, 2007

Mapping of mean imaginary coherence (MIC)

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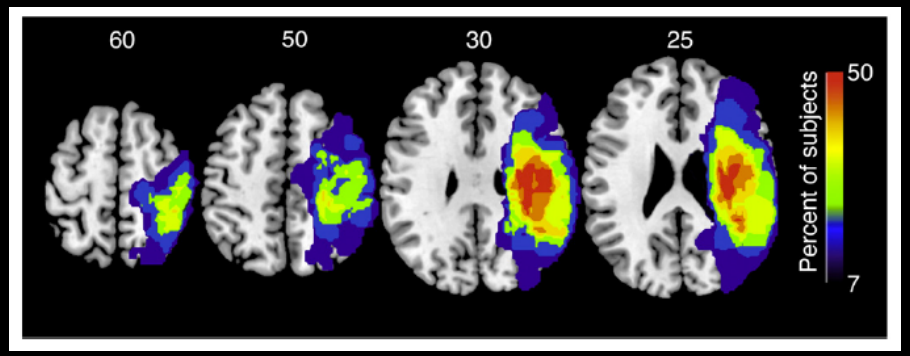
Our working hypothesis

$\bar{\beta}(f, \boldsymbol{r}_j)$ represents communication capability (healthiness) of brain tissue at $\boldsymbol{r}_j$.

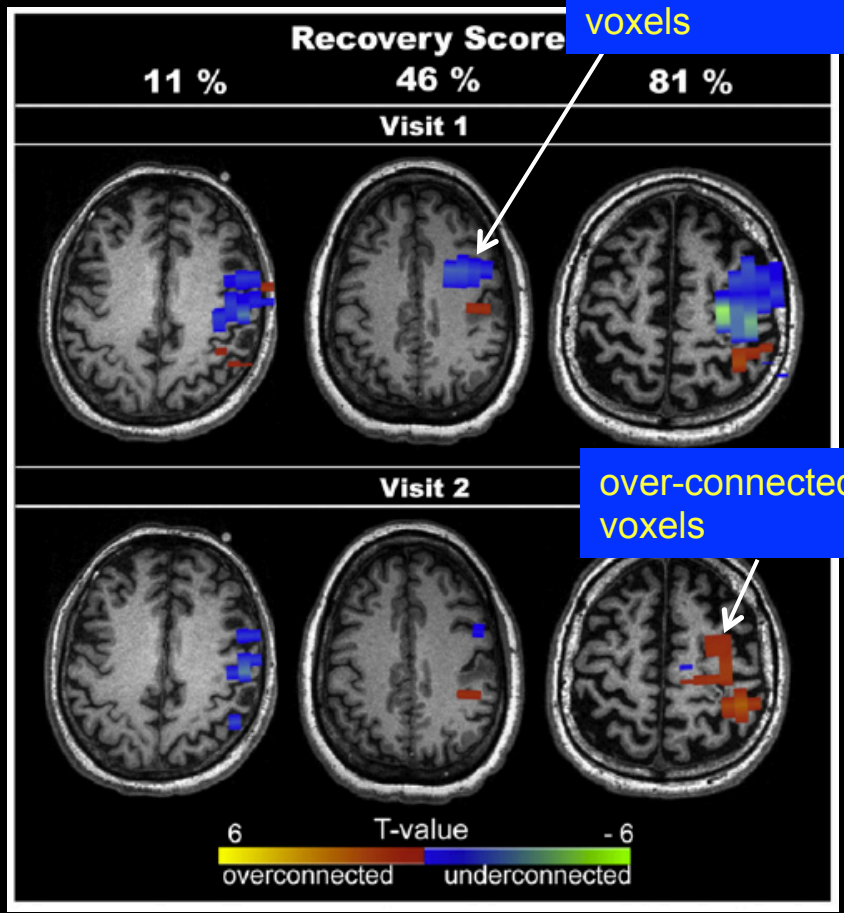
A. G. Guggisberg *et al*., Annals of Neurology, Sep, 2007

Resting state alpha-band functional connectivity and recovery after stroke

- 14 patients with a mono-hemispheric ischemic stroke in the middle cerebral artery affecting the motor output of the hand were selected.
- Mean imaginary coherence map was computed from resting state alpha band MEG.



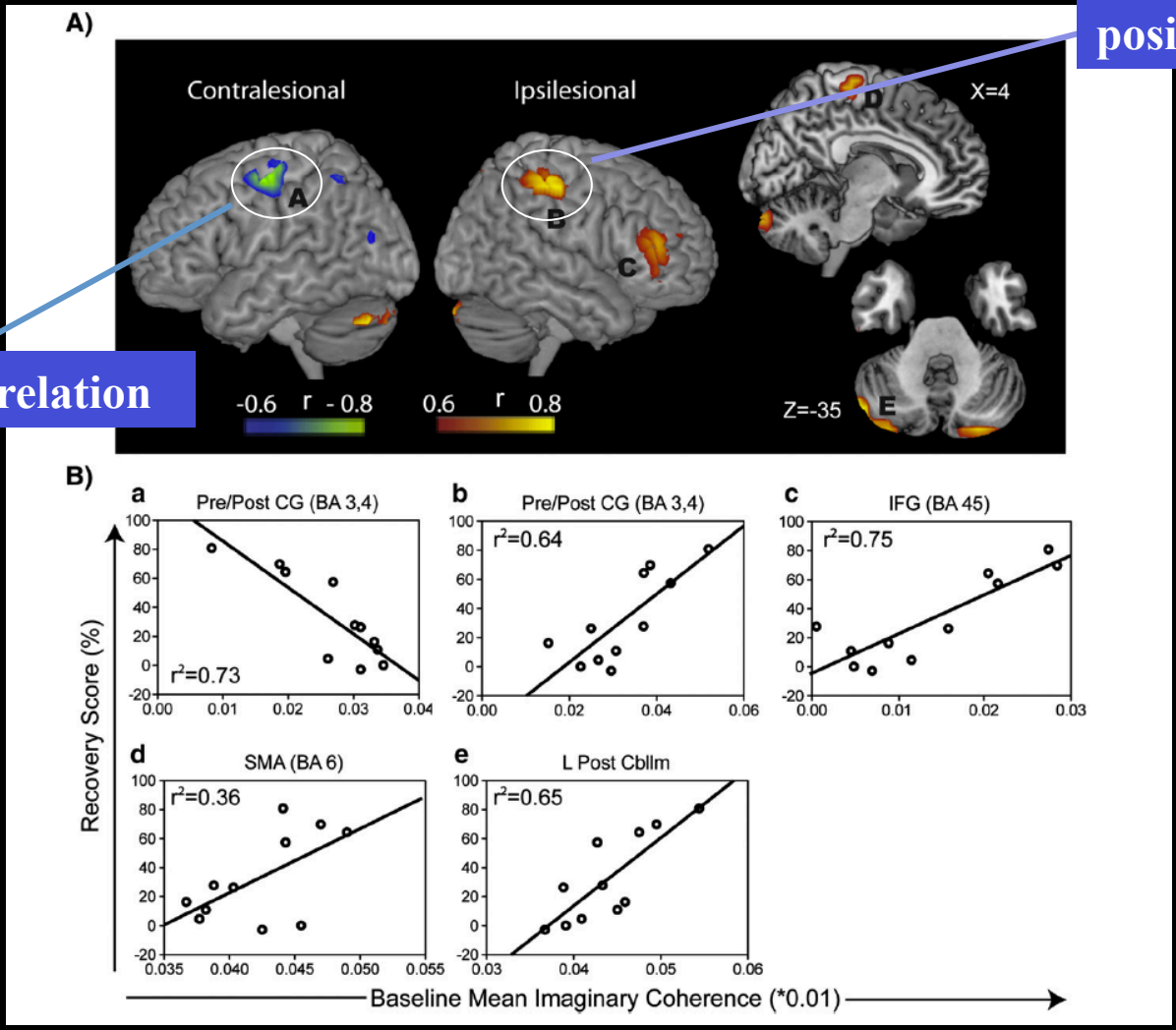
Group lesion overlap map of 14 subjects



Change of mean imaginary coherence image of representative subjects between visits separated by 8-12 weeks.

K. P. Westlake at al. Experimental Neurology 237 160-169, 2012

Correlation with recovery score



positive correlation

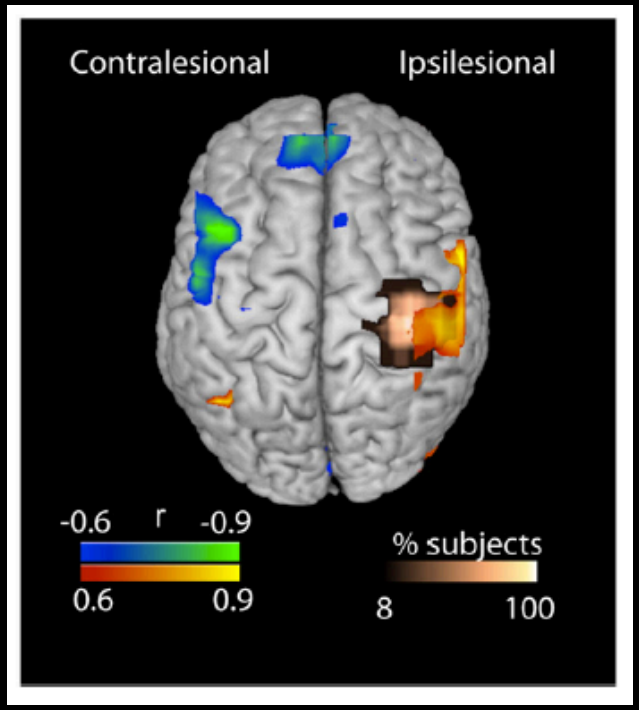
negative correlation

Correlation between mean imaginary coherence and recovery score.

(The correlation is corrected for nuisance parameters such as time post stroke.)

K. P. Westlake at al. Experimental Neurology 237 160-169, 2012

Summary: Correlation between mean imaginary coherence and recovery score:

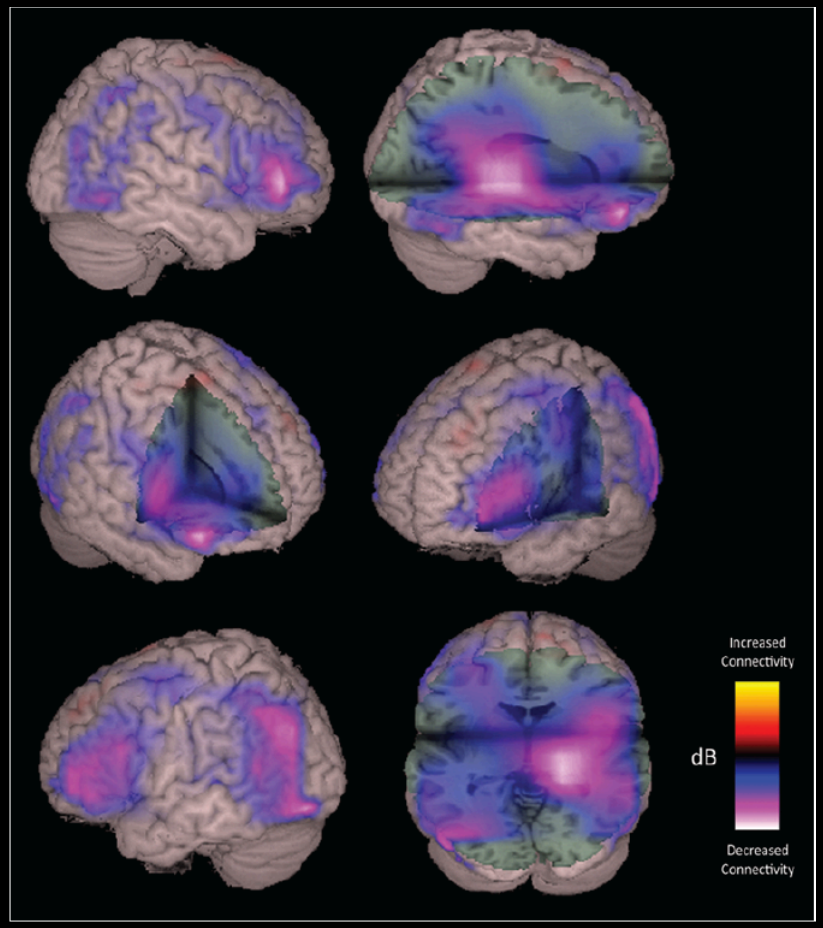


A positive correlation is found near the ipsi-lesional sensorimotor cortex, and significant negative correlation with the contra-lesional sensorimotor cortex.

Values of mean imaginary coherence from the initial MEG session may be able to predict each subject's recovery performance.

If ipsi-lesional and contra-lesional motor areas respectively have high and low MIC values, that patient possibly has a large recovery score.

Resting state alpha-band functional connectivity in traumatic brain injury (TBI) patients



Mean imaginary coherence image from the initial MEG scan

- 21 TBI patients and 18 normal controls.
- Location of the brain damage varies across patients.
- MIC image is computed from resting-state alpha-band MEG.

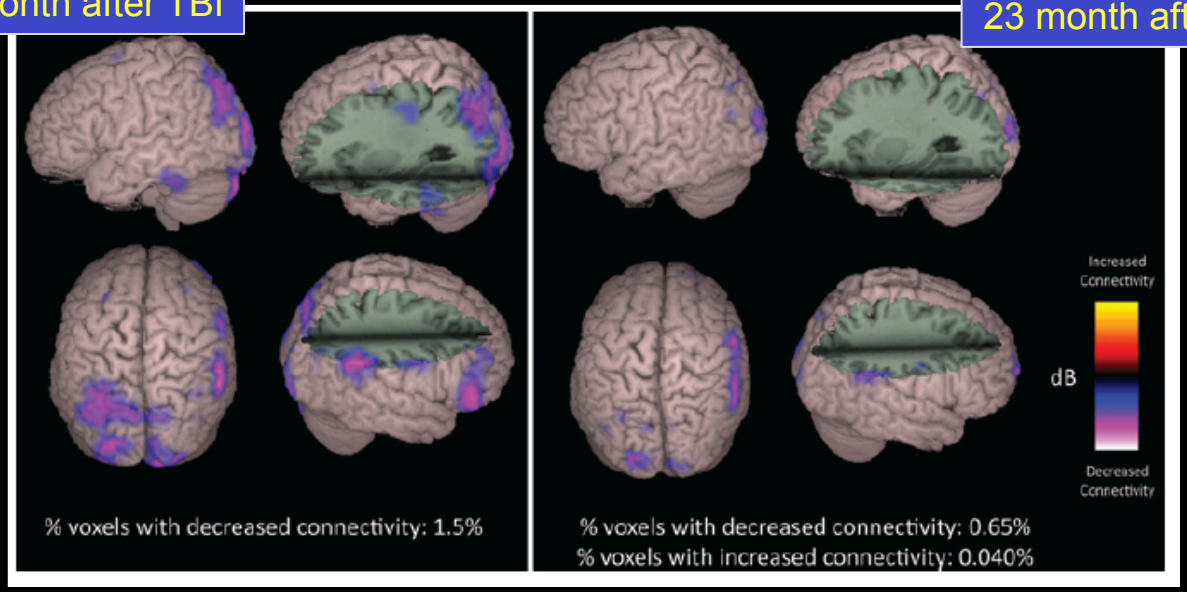
Group comparison between TBI patients and normal controls shows abnormally decreased functional connectivity (regions of under-connected voxels).

P. E. Tarapore, et al. ,J. Neurosurg 118:1306-1316, 2013.

Individual patient cases

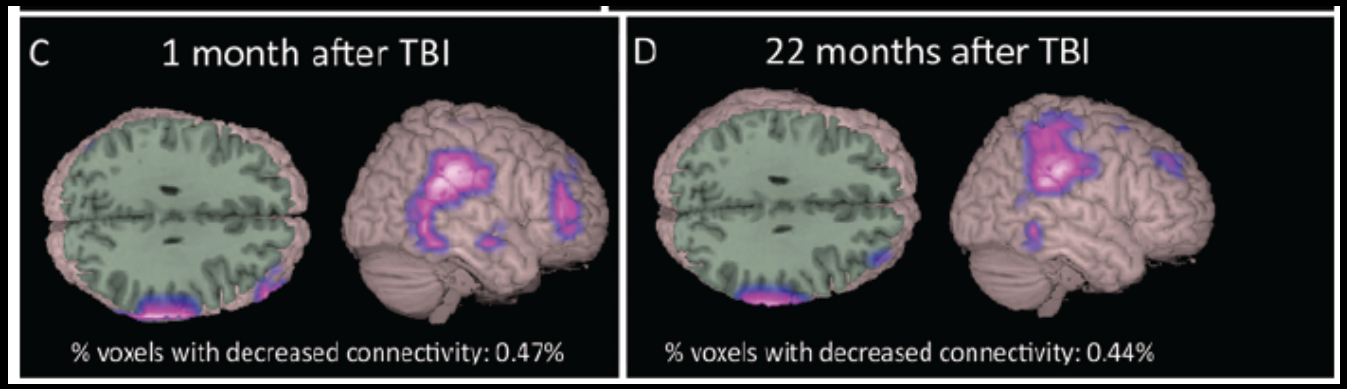
9 month after TBI

23 month after TBI



Significant decrease of under-connected voxels

Results from a patient with a significant recovery



Slight decrease of under-connected voxels

Results from a patient with a slow recovery

Decrease of under-connected (decreased MIC) voxels is in accordance with the patient's recovery

All-voxel-to-all-voxel connectivity analysis

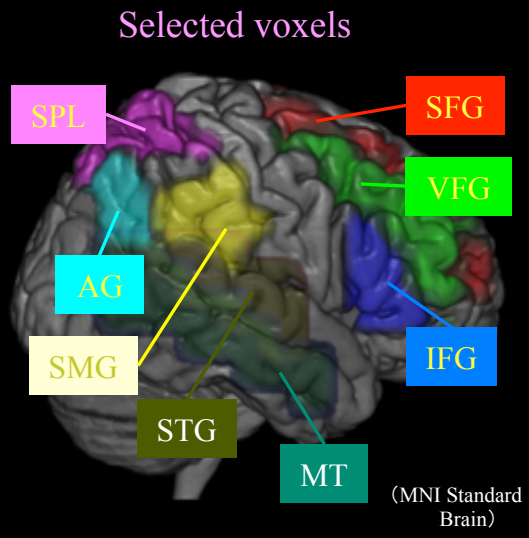
OPEN ACCESS Freely available online

PLOS ONE

Disturbed Resting Functional Inter-Hemispherical Connectivity of the Ventral Attentional Network in Alpha Band Is Associated with Unilateral Spatial Neglect

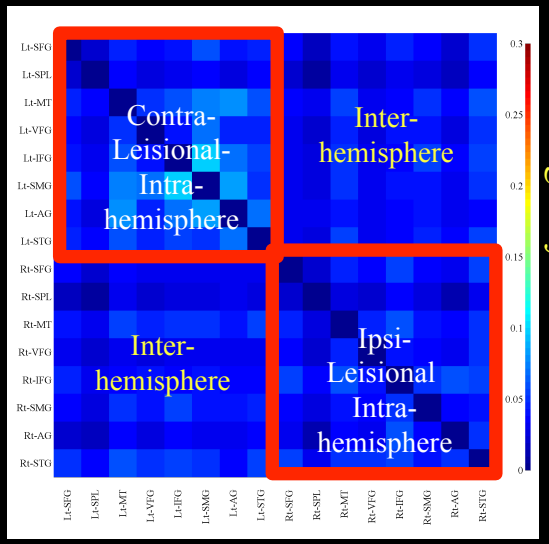
Tsutomu Sasaki[1*], Masayuki Abe[2], Eiichi Okumura[3], Toyoji Okada[4], Kimito Kondo[5], Kensuke Sekihara[6], Wataru Ide[7], Hajime Kamada[7]

- 13 patients with brain damage in their right hemispheres
- 8 patients show USN symptoms(USN+), and 5 patients has no USN symptoms(USN-).
- 5 healthy controls.
- 16 voxels are selected, corresponding to representative brain areas shown here.

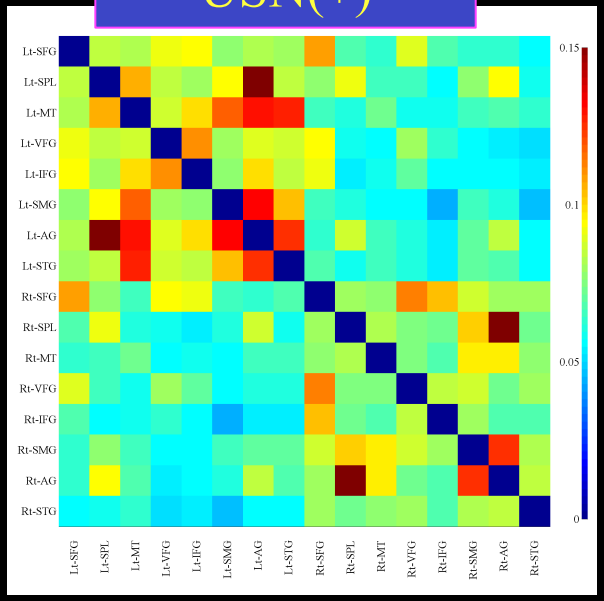


All-voxel-to-all-voxel imaginary coherence matrix is computed using resting state alpha-band MEG.

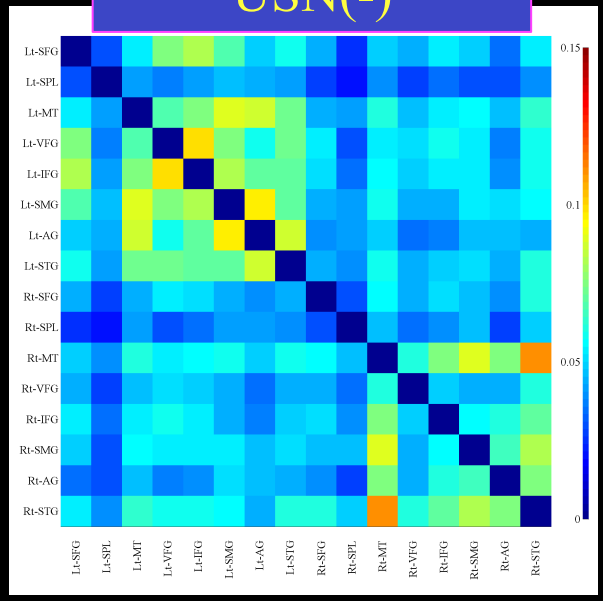
Resting-state alpha-band connectivity: results of all-voxel to all voxel coherence matrix



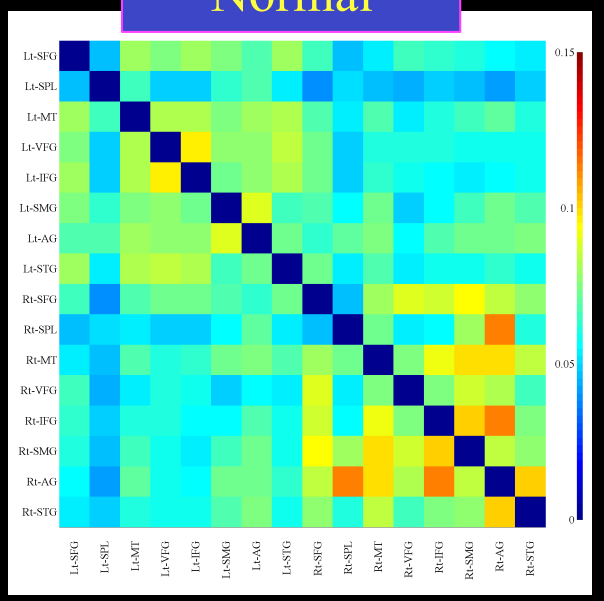
USN(+)



USN(-)



Normal

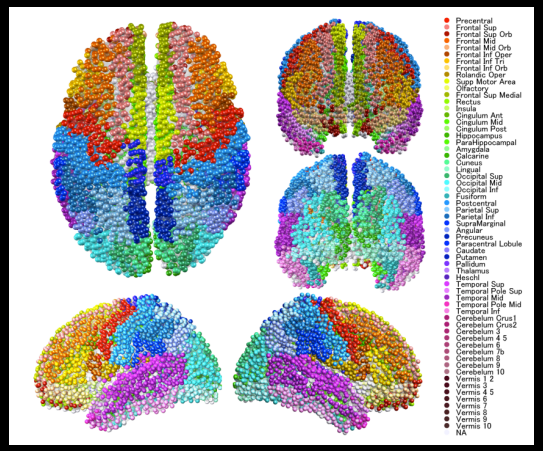


Patients with USN+ have excess intra-hemispheric connectivity, particularly in the contra-leisional hemisphere.

All-voxel-to-all-voxel connectivity analysis applied to schizophrenia patients:

Magnitude vs. imaginary

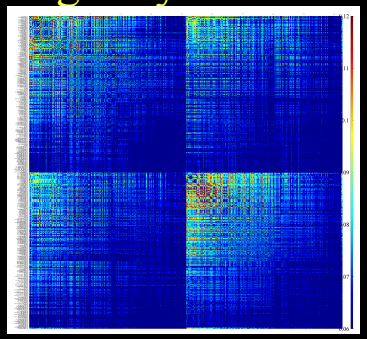
- Resting state.
- 8-13 Hz (alpha band).
- 12 patients, and 12 healthy controls.



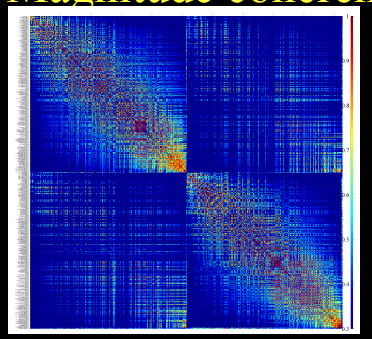
512 voxels assumed in subject's cortex

Patient (grand average)

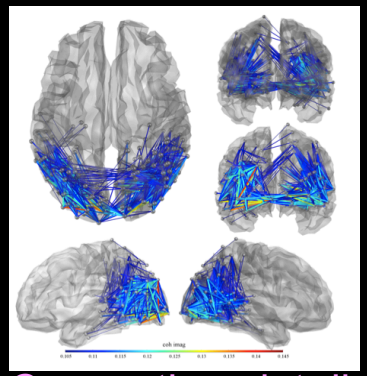
Imaginary coherence

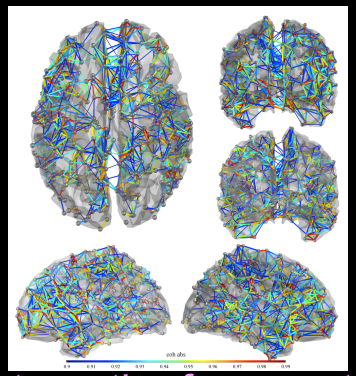


Magnitude coherence



Coherence matrix display



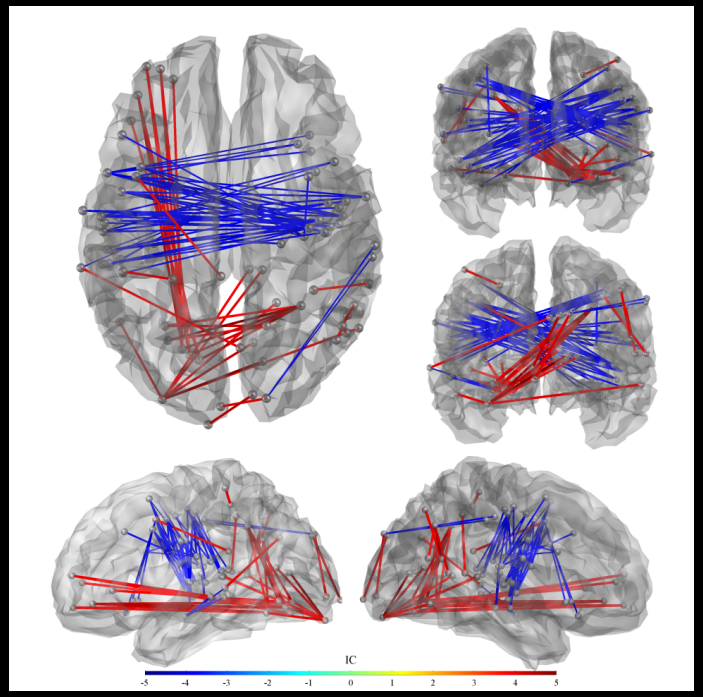


Connection plot display: strength of connectivity is shown by a color-coded line connecting the pair of voxels.

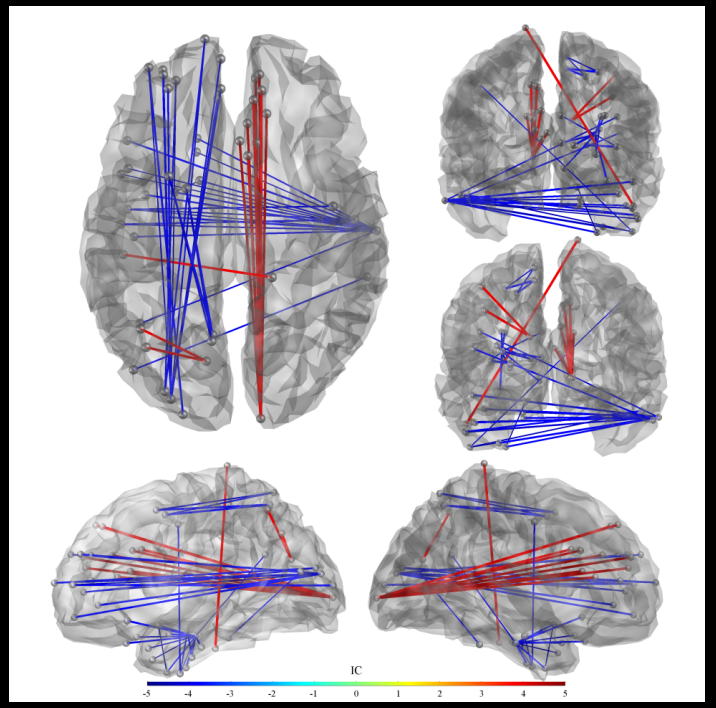
Magnitude coherence matrix contains seed blur, which obscures true interaction. Connection plot for magnitude coherence is not interpretable.

Connection plot: Patient – Control: Two sample t test

Imaginary coherence



magnitude coherence



P > C

C > P

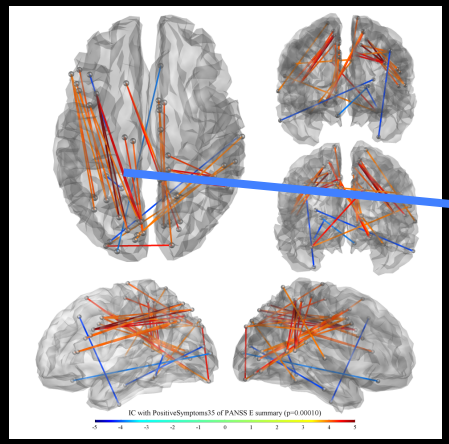
$p < 0.001$

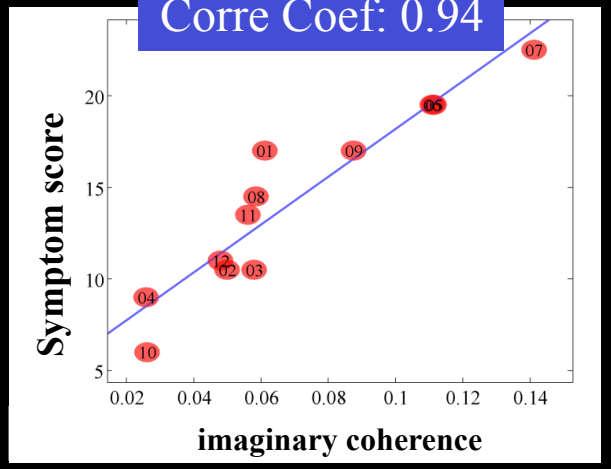
t: 3.7921

- Computing the difference between patient and control can remove the seed blur (spurious coherence) in the magnitude coherence image.
- Magnitude coherence image shows a cortical network different from the one shown in the imaginary coherence image.

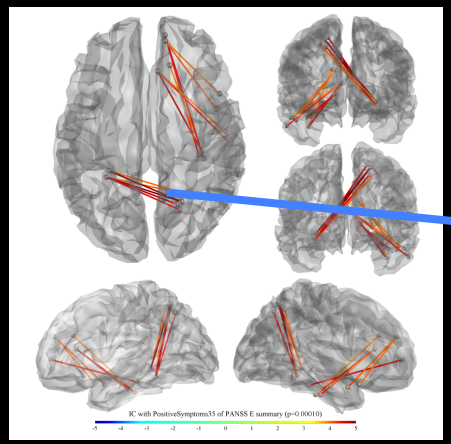
Correlation with symptom scale: positive symptom

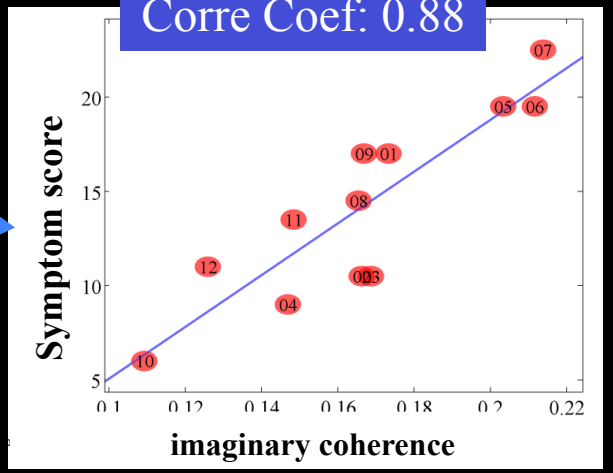
Imaginary coherence





Magnitude coherence





Imaginary(IC) and magnitude coherences(MC) may represent different cortical networks: IC represents connections with some delay, and MC represents instantaneous connections (connections with a small delay).

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Thank you very much for your attention.

Summary

- The methodology of our MEG source space connectivity analysis is described.
- Results of several clinical applications are shown.
- we