Functional Neuroimaging:
The “Dis”-Connectome

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...Will the Connectome Create New Markets...?

The “Connectome” Now on iTunes
Now! The "Armchair" Connectome

NEW YORK, March 11, 2013 -- (NYSE: GE) -- GE and the NFL today announced the Head Health Initiative, a four-year, $60 million collaboration to speed diagnosis and improve treatment for mild traumatic brain injury. The goal of the research and innovation program, guided by healthcare experts, is to improve the safety of athletes, members of the military and society overall.

"Clarity" Drives "BRAIN"

The "Connectome" Magnet- PRISMA

The 2013 "BRAIN" Roadmap

http://www.youtube.com/watch?v=EI-VcvwgCgE

The role of Advanced MR?

TBI and the “Dis-Connectome”
Mod to severe detectable with classic MR methods.

Mild TBI in general has a good prognosis.

But 15 - 30% patients have cognitive, physiological and clinical symptoms at 3 months post injury.

Majority of patients have negative conventional MR.

Identify this group at risk for long term disability and early therapy.

WHY ADVANCED MRI?

http://emedicine.medscape.com/article/344973-overview

TBI Background

Wikipedia

Multi-Contrast MR – Key to the Connectome

Voxel Based Morphometry (VBM) t-test analyses of regional changes over patient populations. Freesurfer/NeuroQuant.

One year after mild TBI, brain atrophy seen anterior cingulate WM bilaterally left cingulate gyrus isthmus WM, right precuneal GM


Frontal Regions Susceptible to Injury

Diffusion Tensor Imaging (DTI)

**Acquisition**

**Reconstruction**

**Modeling**

**Proton Diffusion in GM**

**Proton Diffusion in WM**

One Way to Display DTI: Tractography

Diffusion Pathways

ADC

\[
\begin{bmatrix}
ADC_{xx} & ADC_{xy} & ADC_{xz} \\
ADC_{xy} & ADC_{yy} & ADC_{yz} \\
ADC_{xz} & ADC_{yz} & ADC_{zz}
\end{bmatrix}
\]

Tensor

Y

X Z

Magnet axis

Fiber axis

ADC

FA
DWI vs. DTI: Which is Which?

DWI in Stroke

DWI in Screening CNS

DWI in MSK

DTI in MSK

DTI in Diseases

DTI in CNS disease

Technique Development

DWI "ADC"

DTI "FA"

A Decade of DTI in Traumatic Brain Injury: 10 Years and 100 Articles Later


- The most commonly identified regions of abnormal FA or MD in DTI studies of TBI:
  - Corpus callosum,
  - Frontal lobe,
  - Internal capsule,
  - Cingulum

DTI Modeling and Statistics

DTI Multi-Subject Statistical Apps

http://fsl.fmrib.ox.ac.uk/fslcourse/lectures/fdt.pdf


Automated White Matter Tract Segmentation (TRACULA)

Freesurfer

TRActs Constrained by UnderLying Anatomy

FreeSurfer Module Freesurfer.net

MRIStudio.org

Adult atlas

Pediatric atlas (24M)

Neonatal atlas
**“Higher Order” DTI**

*Why Make This Harder?*

- The number of b values can provide additional data for modeling the microstructure of the brain.
- Conventional DTI sequences tend to use the single b value of 1000, plus some number of b0 images.
- Having additional b value images other than b0 enables a number of different modeling techniques.
  - *Conventional DTI is not enough!*

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**Diffusion Kurtosis Imaging (DKI)**

- Assumes substantially non-gaussian distribution of water diffusion
- May better evaluate diffusion properties outside of highly organized large white matter tracts.

<table>
<thead>
<tr>
<th>T2W</th>
<th>MK</th>
<th>FA</th>
<th>MD</th>
</tr>
</thead>
</table>

(Images of T2W, MK, FA, MD maps with corresponding brain sections)


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**DTI in TBI**

- within 1 year after mTBI exhibited altered DTI- and DKI measures in thalamus and internal capsule (c/w controls)
- > 1 year after mTBI had differences in splenium of the corpus callosum and the centrum semiovale.
- Cognitive impairment was correlated with Mean Kurtosis (MK) in the thalamus and the internal capsule.


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**Higher Order DTI**

**DSI, QSI, RSI – The Ultimate DTI?**

*Diffusion Full-Space Imaging – 150 Directions – 12 minutes minimum*

[Image of diffusion full-space imaging with a network-like structure]

[Link: http://dsi-studio.labsolver.org]

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**Neurite Modeling (NODDI)**

*Neurite Orientation Dispersion and Density Imaging*

[Image of neurite modeling with a 3D brain structure]

[Link: http://dsi-studio.labsolver.org]

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**UCL Package**

[Image of package with brain sections]
Quantitative Susceptibility Mapping

What and Why?

- DTI is a sensitive measure of WM directions/connectivity but needs more work for measuring integrity.
- QSM is faster with higher resolution and 3D for WM mapping.
- QSM natural extension of GRE and is both bleed/WM sensitive.

Microstructural Imaging - QSM

QSM Shows Bleeds Independent of TE

“The total susceptibility of a cerebral microbleed measured by using QSM is a physical property that is independent of echo time.”


Microstructural Imaging - QSM

QSM is Ideal for VBM

Physical Properties of QSM

QSM Image

- Paramagnetic
  - Higher
  - More paramagnetic microstructures
- Diamagnetic
  - Lower
  - More diamagnetic microstructures

Functiona MRI - fMRI

fMRI is BOLD

Fe

 oxyhemoglobin
 0 = 0
deoxyhemoglobin

HbO₂

 diamagnetic
Low ²

Hb

 4 unpaired electrons
paramagnetic
High ²

HbO₂ Hb
**The Brain Does Not Sleep - Resting State fMRI**

<table>
<thead>
<tr>
<th>Primary Motor</th>
<th>Primary Visual</th>
<th>Extrastriate Visual</th>
<th>Intra-temporal/ACC</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a,b,c,d,e,f)</td>
<td>(a,b,c,d,e,f)</td>
<td>(a,b,c,d,e,f)</td>
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</tr>
</tbody>
</table>

**The Other Connectivity**

When compared with DMN patterns in the control group (A), the patient group (B) showed significantly decreased connectivity in the posterior portion (arrowheads) and increased connectivity in the anterior portion (arrows) of the DMN.


**RS-fMRI BOLD Fluctuations**

- **Related to CBV**
- **Related To Network Delays (!)**

**Multispectral Data Fusion**
Structural Connectivity Mapping

- Diffusion Tensor and volumetric images combined to generate connectivity matrices.
- Matrices then converted to graphs representing brain connectivity.

The Connectome – Putting It All Together

- Compared to controls, the graph analysis showed reduced overall connectivity, longer average path lengths, and reduced network efficiency.
- A particular impact of TBI is seen on a major network hub, the posterior cingulate cortex.
- Taken together, these results confirm that a network critical to cognitive function shows a shift away from small-world characteristics.

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The sample consisted of 57 veterans (7 females), mean age of 46.8 yrs. (median: 45.1), 31 mild TBI, 5 moderate TBI and 43 with PTSD.

Glucose metabolism decreased significantly with increasing TBI severity in the right precuneus and left angular gyrus.

VOI analyses with FWE multiple comparison correction at p < .05 confirmed the robustness of the effect.


PET-MR and TBI

Beyond the Connectome – Room for PET?

MicroStructural Imaging

Proton Diffusion can be Measured as the “ADC”
Thalamic Nuclei Evaluation

- Damage to the structural connections of the thalamus is a frequent feature of traumatic brain injury (TBI) and could be a key factor in clinical outcome.

- Multiple thalamic nuclei atlases available.