Quantitative MRI of the Brain: Investigation of Cerebral Gray and White Matter Diseases

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Quantities Measured by MR - 1

- Static parameters (influenced by molecular environment):
  - T2, T2* (transverse relaxation)
  - T1 (longitudinal relaxation)
  - Proton Density (tumor, stroke, etc)
  - Spectroscopy (metabolite concentrations)

Quantities Measured by MR - 2

- Dynamic parameters:
  - Angiography
  - Diffusion
  - Perfusion

Quantities Measured by MR - 3

- Quantifying changes in tissue morphology:
  - Local and global volumetric measurements
    - » Growth, swelling or atrophy in GM
  - Diffusion Tensor Imaging (DTI)
    - » Microstructural changes in WM, tracking white matter fibers

Quantifying Changes in GM

- Investigate:
  - The developing brain
  - The aging brain (MCI, AD)
  - Brain injury (Traumatic brain injury, etc)
  - Brain morphology in neurological disorders (ADHD, schizophrenia, etc)
- Techniques:

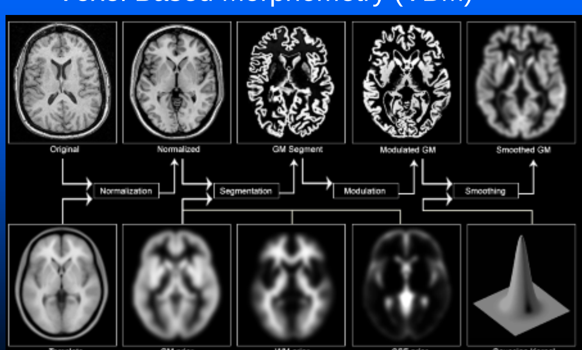
1. Voxel Based Morphometry (VBM)
2. Cortical Surface Measurements
3. Deformation Based Morphometry

Quantifying Changes in GM

Voxel Based Morphometry (VBM)

VBM to Quantify Changes in GM

- Voxel Based Morphometry (VBM)



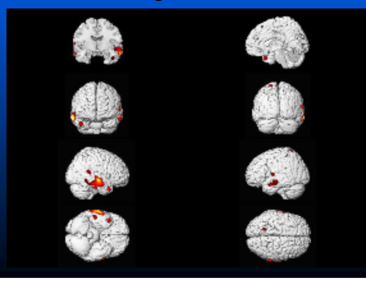
Hobbs & Novak 2007 SPM lecture notes

VBM to Quantify Changes in GM

- VBM statistical analysis
  - If a region has atrophy, those voxels have to be "warped" more to match the template.
    - » Voxel intensities are modulated by the amount of deformation → voxels get darker
  - Apply voxel-by-voxel statistics (T-test, ANOVA, etc) to test group differences in GM volumes

VBM to Quantify Changes in GM

- VBM results:
  - Children; ages 6-9 (N=100)
  - Positive correlation between GM Volume and Gestational age at birth

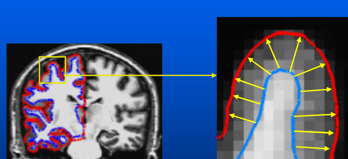


Quantifying Changes in GM

Cortical Surface Measurements

Thickness to Quantify Changes in GM

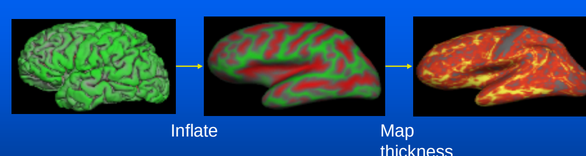
- FreeSurfer: http://surfer.nmr.mgh.harvard.edu



Segment GM and calculate thickness

Thickness to Quantify Changes in GM

- FreeSurfer: Cortical inflation & thickness



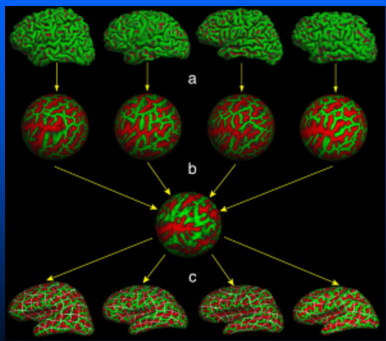
$$J_d = \frac{1}{4V}\sum_{i=1}^{V}\sum_{n\in N(i)}(d_{in}^t - d_{in}^0)^2,\ d_{in}^t = \|\mathbf{x}_i^t - \mathbf{x}_n^t\|$$

1. Tessellate the surface into small triangles.
2. Map each vertex onto the surface
3. Minimize the energy functional to preserve original geometry

*Fischl et al. NeuroImage **9,** 195–207 (1999)*

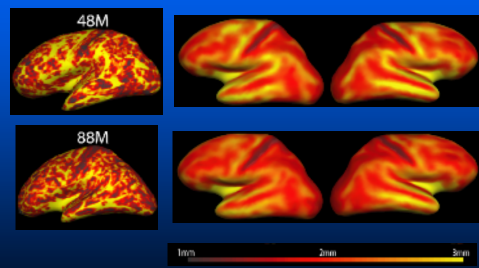
Thickness to Quantify Changes in GM

- FreeSurfer: spatial registration



Thickness to Quantify Changes in GM

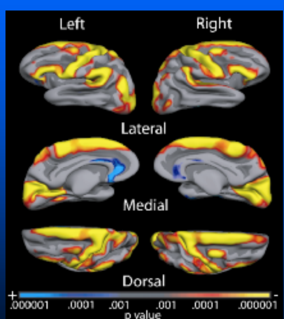
- FreeSurfer: Group mean thickness for 48y and 88y old males



Salat et al., Cerebral Cortex, 14:712-730 (2004)

Thickness to Quantify Changes in GM

- FreeSurfer: Age related thinning in GM



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Quantifying Changes in GM

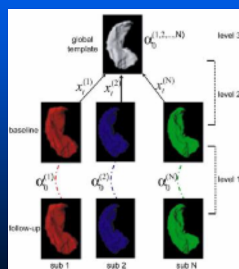
Deformation Based Morphometry

Deformation Based Morphometry

- Large Deformation Diffeomorphic Metric Mapping (LDDMM) *cis.jhu.edu/software*

Hippocampal assessment:

1. Calculate the deformation α_0: follow-up scan $\rightarrow$ baseline scan.
2. Calculate the deformation x_t: baseline scan $\rightarrow$ global template.
3. Transform: follow-up scan $\rightarrow$ baseline scan.



Deformation Based Morphometry

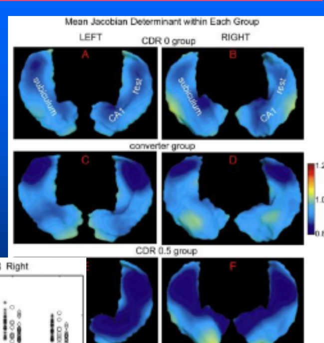
Subjects:

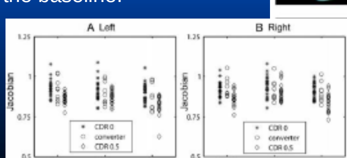
- **CDR 0 group:** Non-demented subjects. 12 males and 14 females. Age: 73 +/- 7.0. The scan interval was 2.2 years (range 1.4 - 4.1 years).
- **CDR 0.5 group:** Mild dementia. 11 males and 7 females. Age: 74 +/- 4.4. The scan interval was 2.0 years (range 1.0 - 2.6 years).
- **Converter group:** CDR0 $\rightarrow$ CDR0.5. 2 males and 7 females. Age: 79 +/- 8.7. The scan interval was 2.8 years (range 1.8 - 4.3 years).

Deformation Based Morphometry

Results:

Jacobian determinant of within-subject deformation between two time points on the global template was computed to indicate hippocampal atrophy (<1) or expansion (>1) in the follow-up relative to one in the baseline.



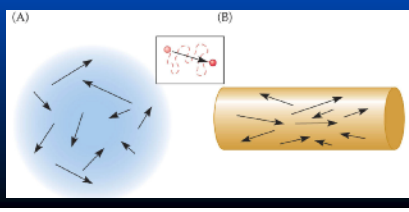


Quantifying Changes in WM

Diffusion Tensor Imaging

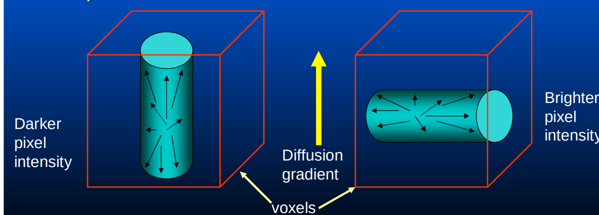
Diffusion Weighted Contrast

- Random translational motion of molecules that can be measured by MRI.
- In media where motion is restricted by borders, the molecules that reach these borders reflect back and diffusion distance is restricted.



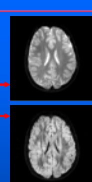
Diffusion Weighted Contrast

- Apply gradient magnetic fields to quantify the amplitude and direction of diffusion.
- Proton spins diffusing in the direction of a magnetic field gradient gain phases
  - Spins diffusing along random paths within a voxel lose phase coherence and lead to destructive interference.



Diffusion Weighted Contrast

- Acquire two MR images:
  - S_0: image with no DW gradient
  - S_1: image with DW gradient



$$S_1/S_0 = exp(-b*D)$$

- b and D lead to attenuation of voxel intensities.
  - b: determined by gradient amplitude and timing D: diffusion coefficient (tissue property).

Diffusion Tensor Imaging

- Multiple DWI are collected with non-collinear gradient directions
- b becomes a vector of gradient directions

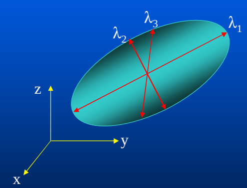
$$\frac{S}{S_0} = \exp\{-(\vec{b})^{1/2} \cdot \bar{\bar{\mathbf{D}}} \cdot [(\vec{b})^{1/2}]^T\}$$

Diffusion tensor matrix: $$\bar{\mathbf{D}} = \begin{bmatrix} Dxx & Dxy & Dxz \\ Dyx & Dyy & Dyz \\ Dzx & Dzy & Dzz \end{bmatrix}$$

- $\bar{\mathbf{D}}$ can be estimated using least squares techniques.

Diffusion Tensor Imaging

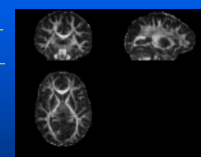
- Apply diagonalization to $\overline{\overline{\mathbf{D}}}$:
  - Three eigenvectors, v_1, v_2, v_3
  - Three eigenvalues λ_1, λ_2, λ_3



DTI scalar maps: Quantify Morphology

- Fractional anisotropy (FA)
  - How much does the local diffusion deviate from a isotropic diffusion?

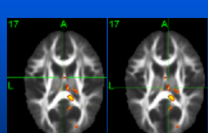
$$FA = \sqrt{\frac{1}{2}}\frac{\sqrt{(\lambda_1-\lambda_2)^2+(\lambda_2-\lambda_3)^2+(\lambda_1-\lambda_3)^2}}{\sqrt{(\lambda_1{}^2+\lambda_2{}^2+\lambda_3{}^2}}$$



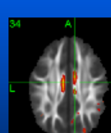
- Other common scalar maps: Mean Diffusivity, Radial Diffusivity, λ_1

DTI applications

- Correlation of FA with gestational age at birth



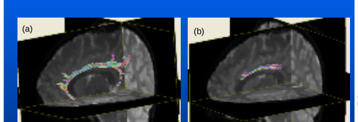
Fornix: WM fiber connecting to hippocampi



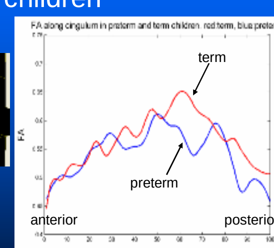
Cingulum: WM fiber connecting memory and learning circuitry

DTI applications: Tractography

- Quantify DTI metrics in the cingulum of preterm and term born children



(a) Left Cingulum. (b) Segment of cingulum used in group comparisons.



(c). Plot of FA along cingulum segment of fig.(b) averaged over term (red) and preterm (blue) children. The standard deviation was 0.045. The error bars were excluded for visual clarity.

Suggested reading

- *Quantitative MRI of the Brain*. Paul Tofts (Ed.). John Wiley & Sons Ltd. 2003

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