Quantitative Analysis of Medical Imaging Data in R

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Outline

Motivation
Task View
Case Studies
fMRI
DTI
PET
Opportunities
End

1. Motivation
2. Medical Imaging Task View
3. Case Studies
   - Functional MRI
   - Diffusion Tensor Imaging
   - Positron Emission Tomography
4. Opportunities
5. Conclusions

The Drug Development Process

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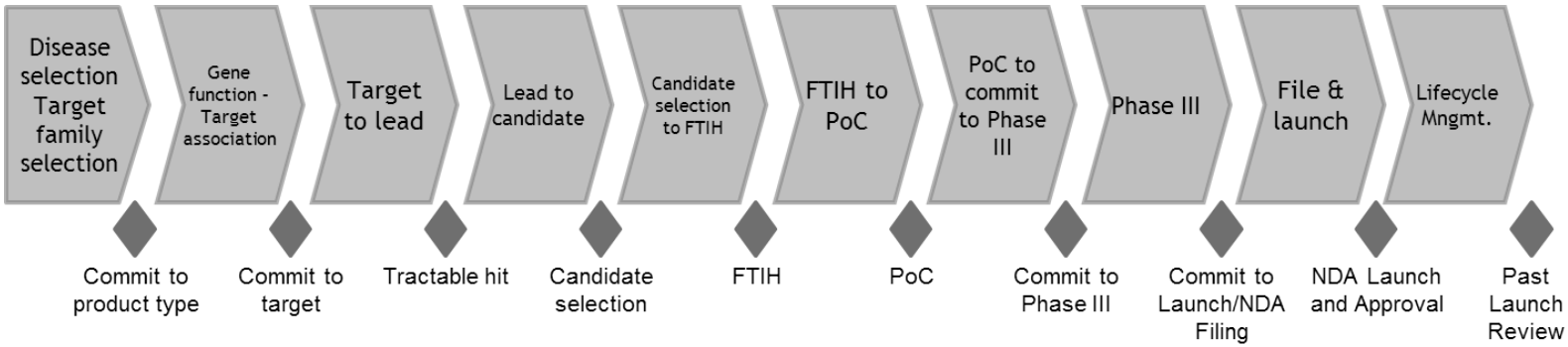

- New drug development can take from 10-20 years with an estimated average of about 9-12 years.
- The best estimate of the costs of drug R&D today is likely to be that from the most recently available well-designed study; that is, USD 802 million.

Dickson & Gagnon (2009; Discovery Medicine)

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Medical Image Analysis for Drug Development

- Quantitative image analysis and statistical inference.
- Application development, validation and deployment.
- Translational imaging: pre-clinical and clinical studies.
- Work with clinical scientists to determine suitable imaging biomarkers.
- Work with medical physicists to determine appropriate image acquisition guidelines.

Three stages of a clinical imaging study.

- Setup
- Operations
- Analysis

The R Project for Statistical Computing

- **R** is a free software environment for statistical computing and graphics.
- **R** compiles and runs on a wide variety of UNIX platforms, Windows and MacOS.
- Package development places the burden on the developer, not the user.

How do you analyze your data?

- Free / proprietary software.
- The best tool for the job.
- Write it yourself.

Programming environments?

- Matlab ITK Python IDL **R** C++ Fortran C#

Medical Imaging Task View

- Operational for 3+ years now
- 15 packages
- 3 projects
- Modalities = EEG, MRI, PET and data formats

Volume 44 of the *Journal of Statistical Software*

Special volume on "Magnetic Resonance Imaging in **R**"

- 13 articles on structural fMRI, fMRI, DTI, DCE-MRI, connectivity, etc.
- `www.jstatsoft.org/v44`

- New packages are always welcome!

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Functional MRI: Example

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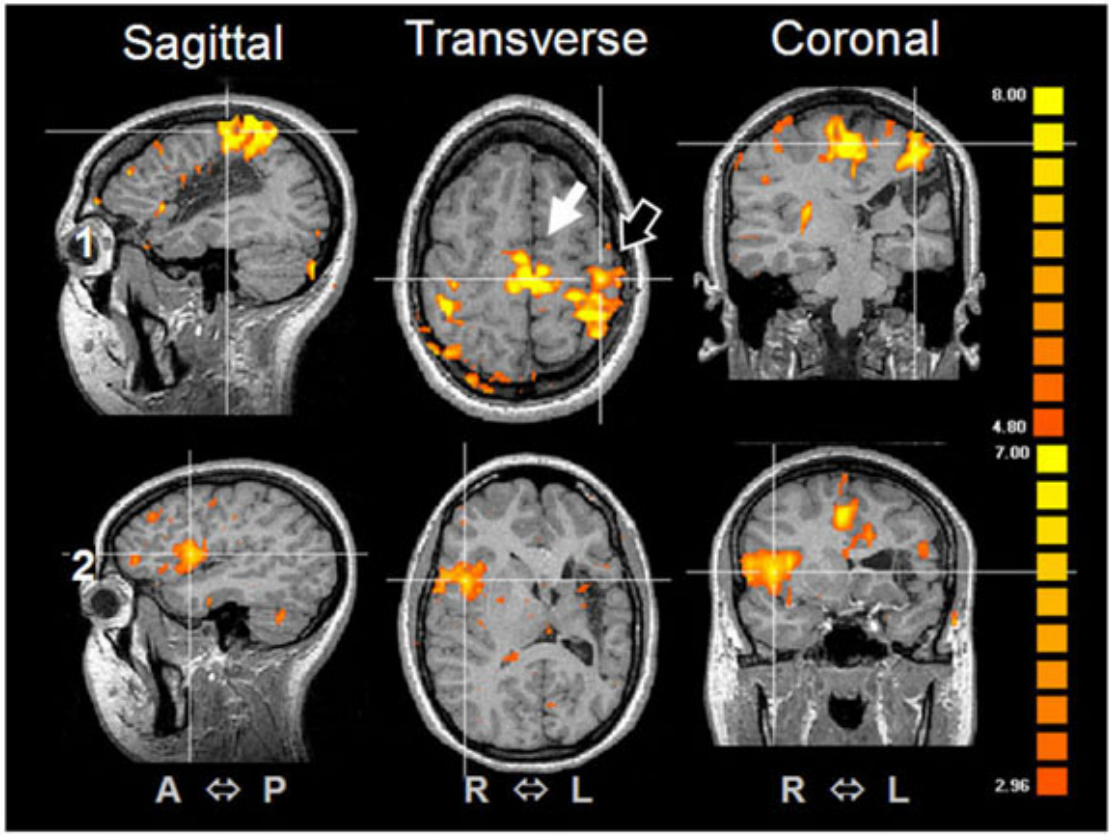

Figure 1. Functional MRI showing on the roll 1 a finger typing motor task with primary motor cortex (Brodman area 4, Outlined White Arrow) and supplementary motor area activation (Brodman area 6, Bold White Arrow). There is a tiny activation on the contralateral primary motor cortex, either. On the roll 2 one can see a robust activation on the homolog Broca area, on the right inferior frontal gyrus. Note the destructive lesion on the left frontal lobe.

Junior *et al.* (2009; J Epilepsy Clin Neurophysiol)

Functional MRI: **fmri** example

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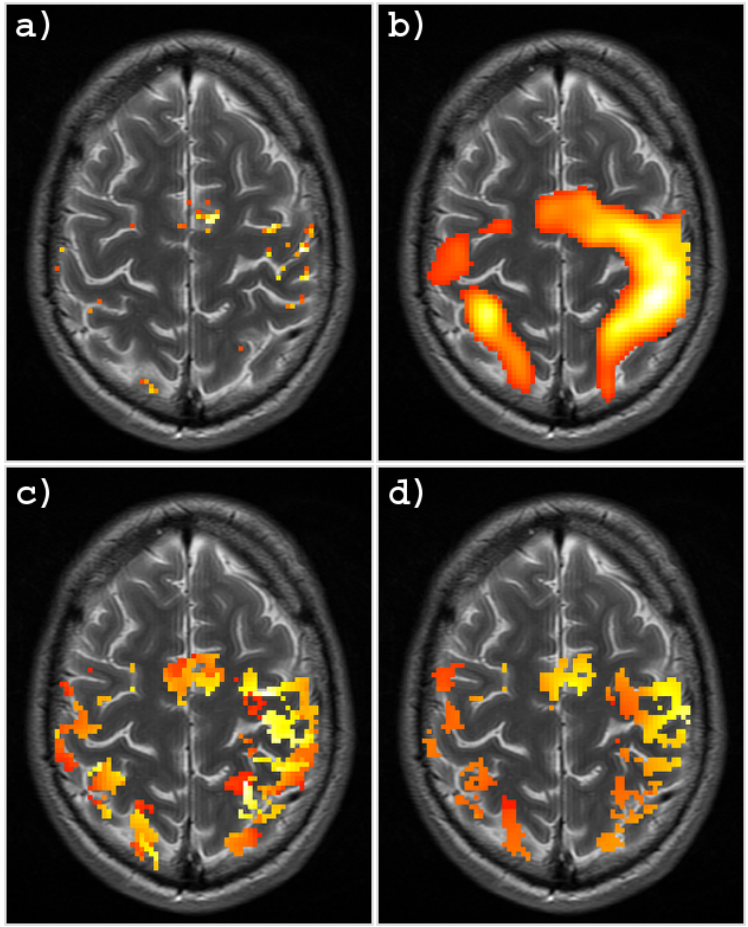
Package **fmri** using different smoothing methods (corrected *p*-value = 0.05).

- a) No smoothing
- b) Gaussian smoothing
- c) Structural adaptive smoothing and Random Field Theory
- d) Structural adaptive segmentation



Tabelow *et al.* (2011; NeuroImage)

Functional MRI: Software

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The Big Guns

- FMRIB Software Library (FSL) [license?]
- Statistical Parametric Mapping (SPM) [GPL $\geq$ 2]
- Analysis of Functional NeuroImages (AFNI) [GPL $\geq$ 2]

Medical Imaging Task View

- **AnalyzeFMRI**
- **arf**
- **cudaBayesreg**
- **fmri**
- **neuroim**

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Diffusion Tensor Imaging: Example

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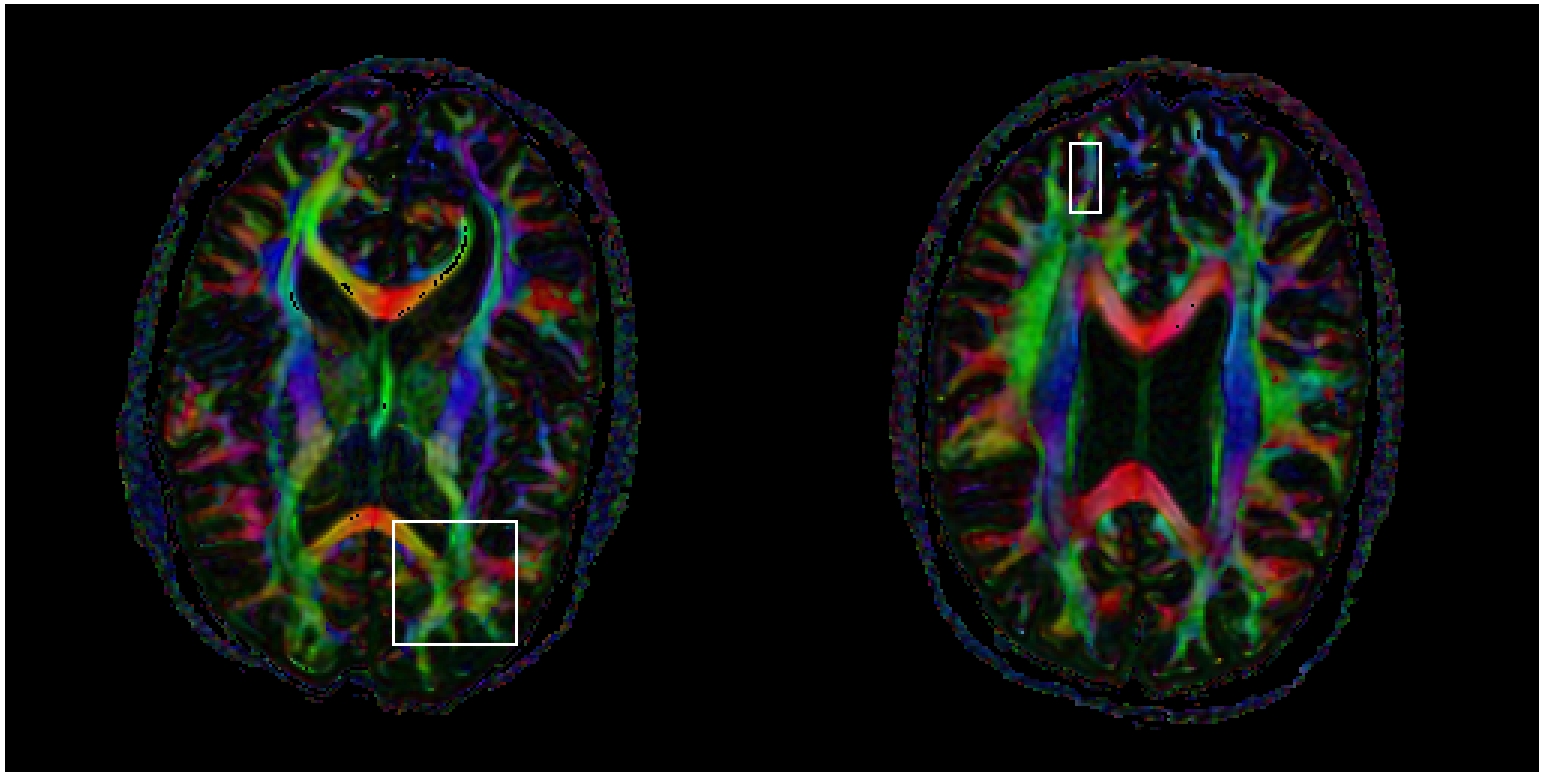

Polzehl and Tabelow (forthcoming)

Tractography: Example

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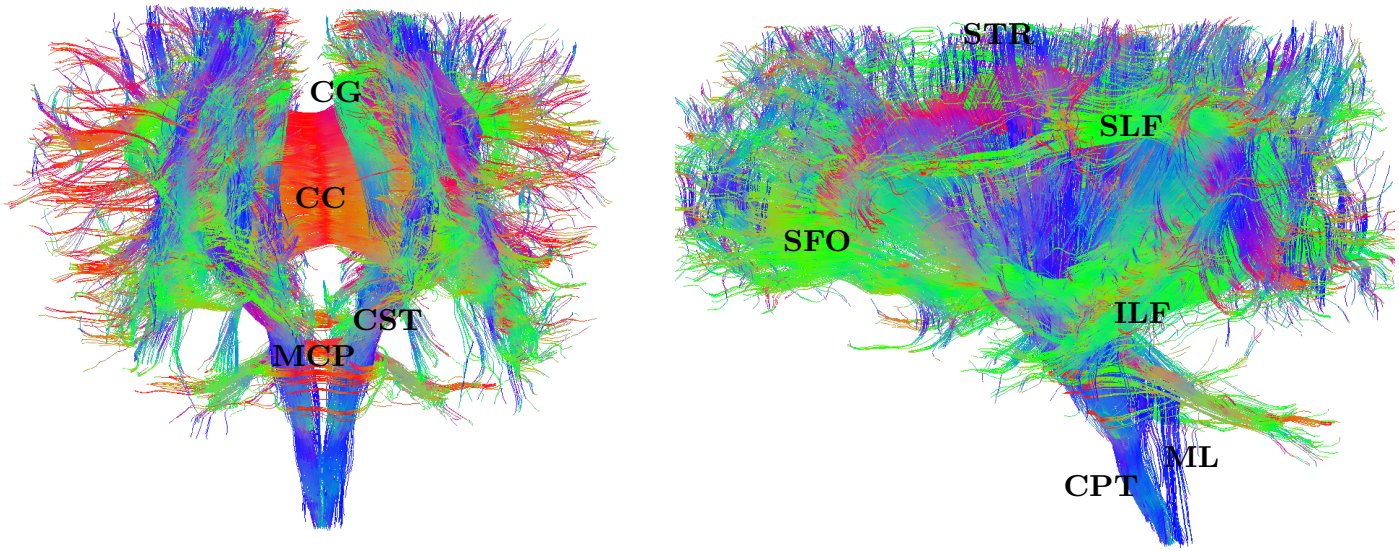

Polzehl and Tabelow (forthcoming)

Diffusion Tensor Imaging: Software

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The Medium-Sized Guns

- FMRIB Software Library (FSL) [license?]
- SPM Extension(s)
- AFNI plugin?
- Camino Diffusion MRI Toolkit [license?]
- DTIStudio [license?]
- (please do not be offended if your software is not listed)

Medical Imaging Task View

- **dti**
- **tractor.base** (part of TractoR project)

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Compartmental Models in PET

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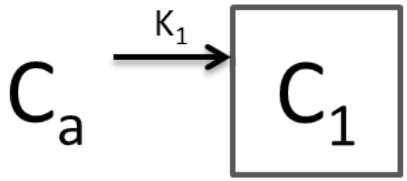
A



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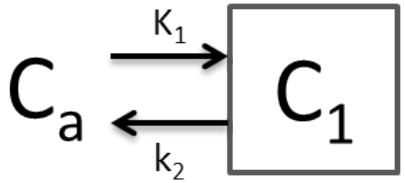

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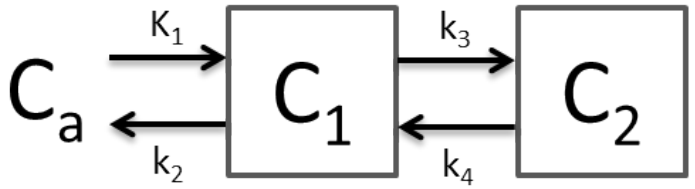

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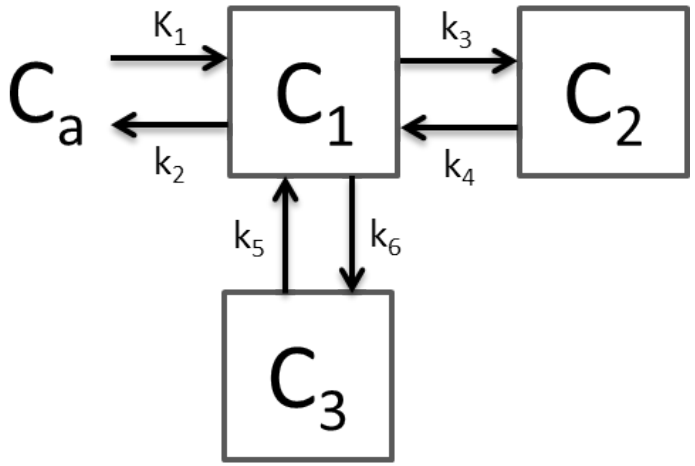
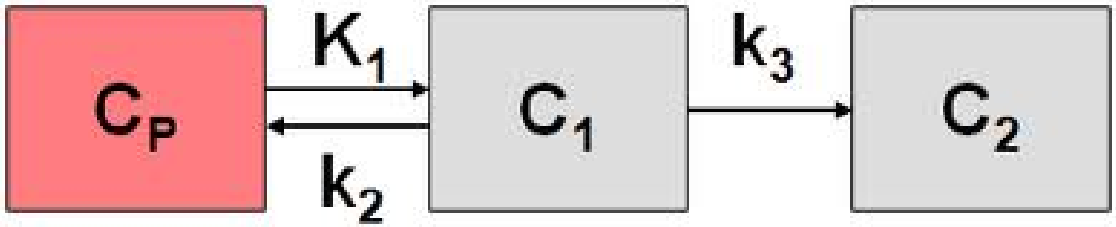


FDG-PET

The Sokoloff Deoxyglucose Model

$$\text{CMR}_{\text{glu}} = \frac{[\text{glucose}]}{\text{LC}} \times \frac{K_1 k_3}{k_2 + k_3} = \frac{[\text{glucose}]}{\text{LC}} \times K_i$$

- [glucose] = circulating glucose level (μmoles/ml)
- LC = "lump constant"



The lumped constant (Sokoloff *et al.* 1977) accounts for the differences in transport and phosphorylation rates between D-glucose and 2-fluoro-2-deoxy-D-glucose.

FDG-PET & Dementia

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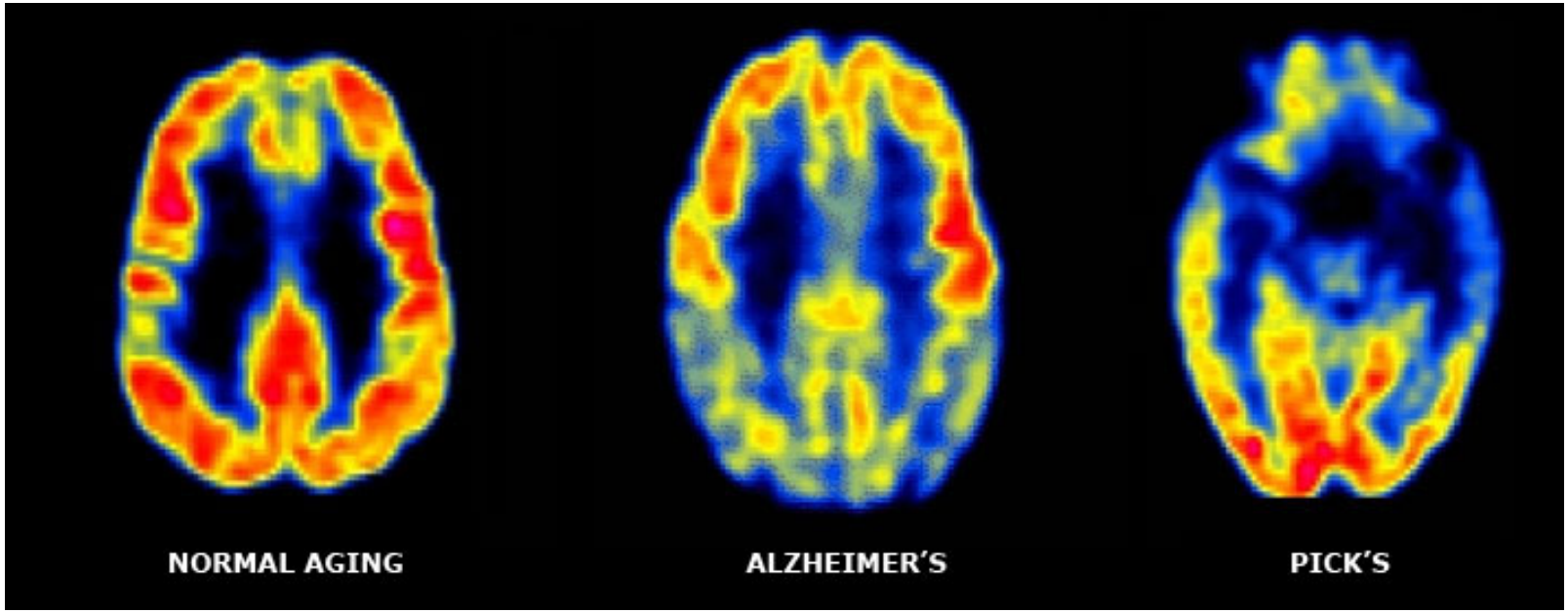

Figure 2. FDG PET images showing patterns of metabolic activity that are characteristic of patients with Alzheimer's disease, Pick's disease (fronto-temporal dementia) and elderly individuals with no dementia. Red, high FDG uptake, Blue, low FDG uptake.

Miller (2004; Radiology Rounds)

FDG-PET vs. [11C]PiB-PET

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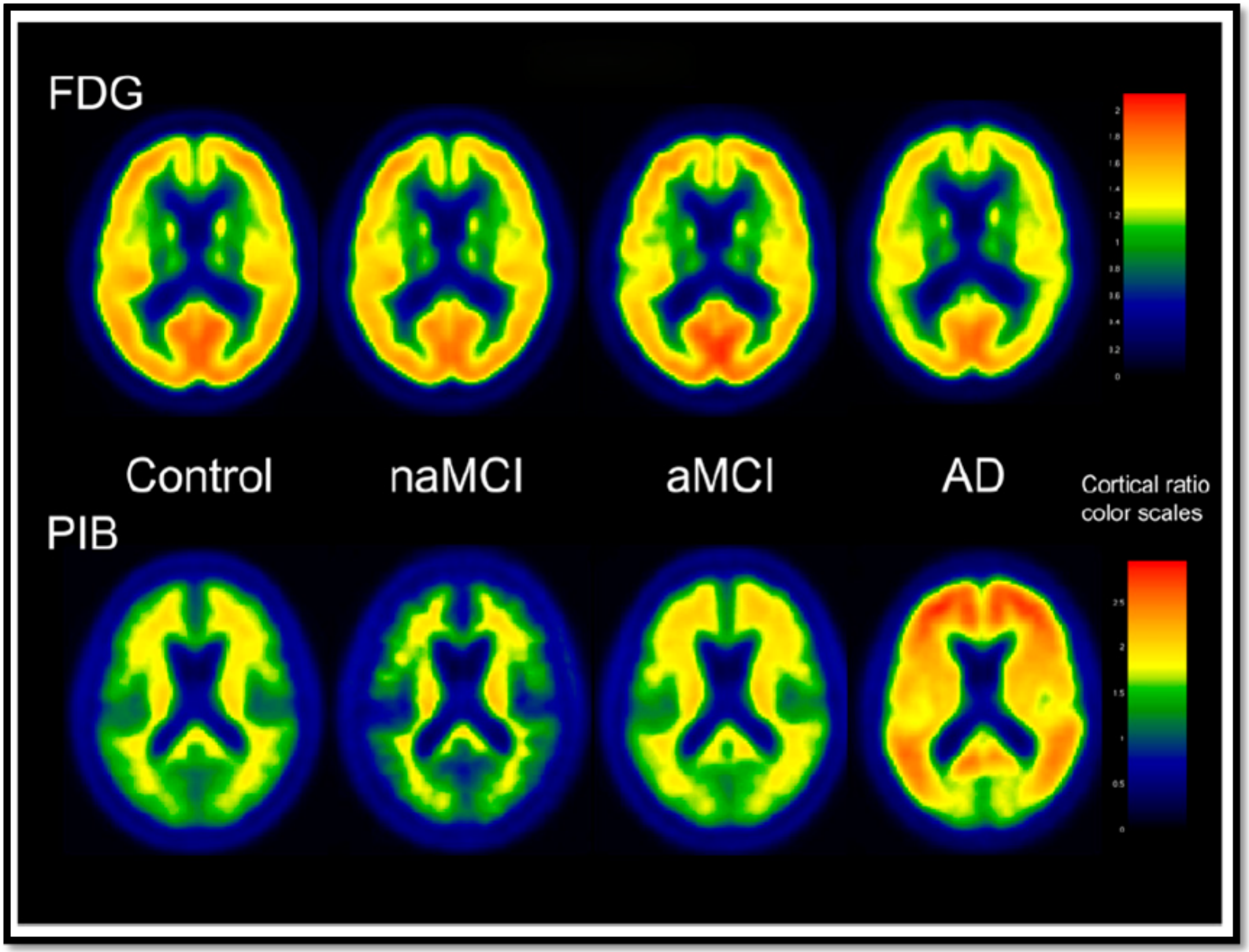

Patel (2011; Presentation)

Positron Emission Tomography: Software

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Where is my gun?

- Statistical Parametric Mapping (SPM)
- PMOD (`http://www.pmod.com`) [proprietary]

Medical Imaging Task View

- **PET** (reconstruction only)
- **oro.pet** (not yet released)

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Image Analysis

- Pre-processing
  - (Non)Linear Registration (**RNiftyReg**)
  - Segmentation, Normalization

Third-Party Libraries?

- Insight Segmentation and Registration Toolkit (ITK)
- Visualization Toolkit (VTK)
- NiftyReg

R Gurus wanted to help create **RITK** package

- SimpleITK is a new C++ layer on top of ITK
- If interested, please contact me!

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Data Formats

- **R** packages that access DICOM / ANALYZE / NIfTI
  - **AnalyzeFMRI**
  - **fmri**
  - **oro.dicom**, **oro.nifti**
  - **Rniftilib**
  - **tractor.base**

Question #1

What are the (dis)advantages to having a single **R** package that performs input / output for medical imaging data?

Question #2

Should **R** packages be discouraged from writing output in formats other than ANALYZE or NIfTI?

Summary

- Open-source / public-domain software and data sets are key to incrementally improving the quality of the methodology and implementation of algorithms applied to (pre-)clinical studies.
  - Clinical research
  - Drug development
- Medical image analysis benefits from statisticians and physicists working together.
  - Signal processing & Image processing
  - Group-level analysis & Statistical inference
  - Genetics + Neuroimaging
- New methodology versus basic functionality
  - Intended audience?
  - Purpose of the software?
- Please consider **R** for future research and software development.

I would like to thank

- R-core team, CRAN, R-Forge, R-community, ...
- Current members of the Medical Imaging Task View
- Future members of the Medical Imaging Task View
- My collaborators

Thank-you