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Beyond 256 shades of grey: Quantitative MRI for probing brain microstructure

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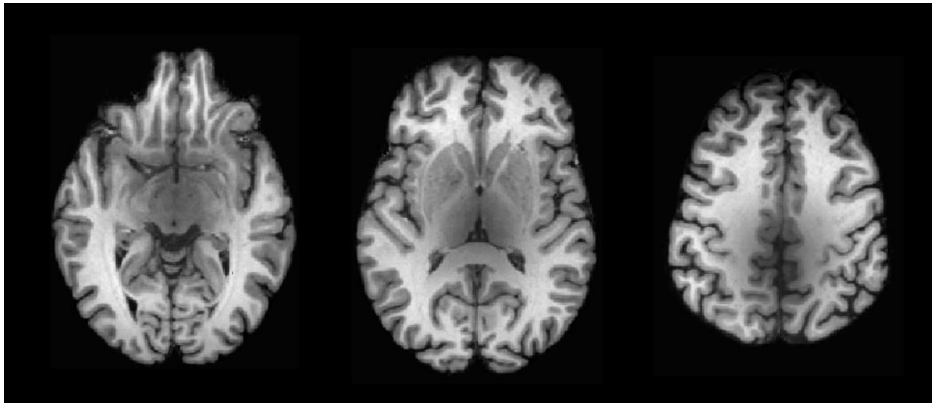
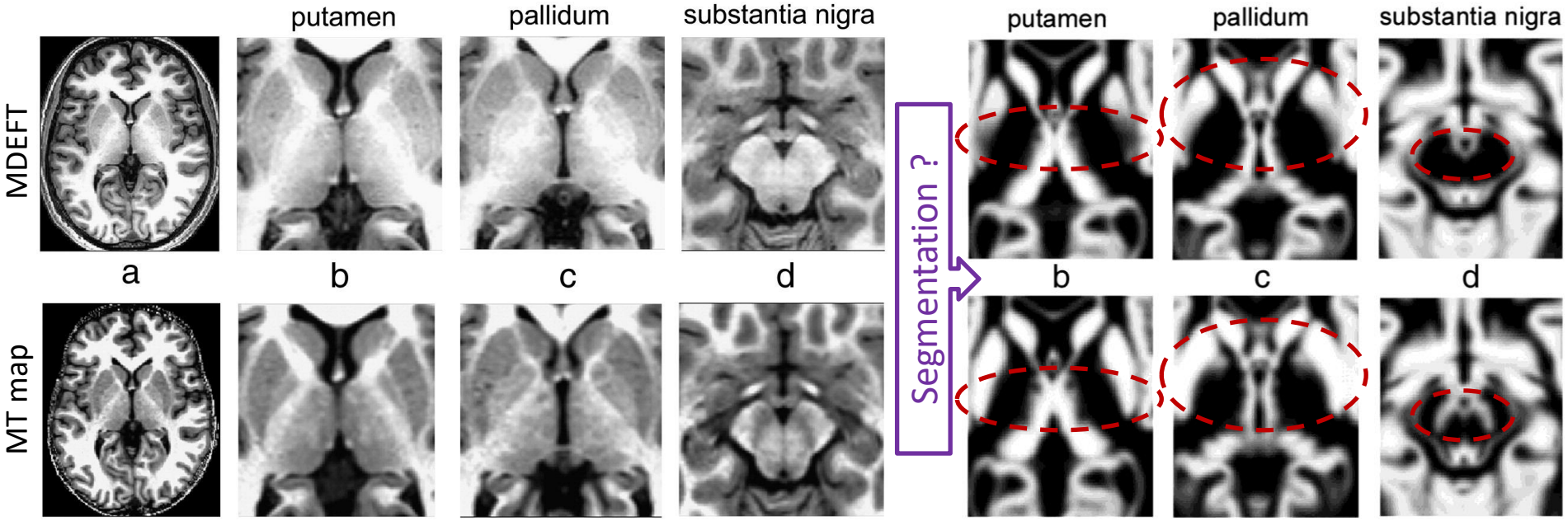
Studying structural organisation & plasticity?

- T1-weighted MPRAGE image
- Observe differences across groups or changes over time



⇒ Macroscopical changes observable via **morphological changes** (i.e. in GM density, cortical thickness,…)

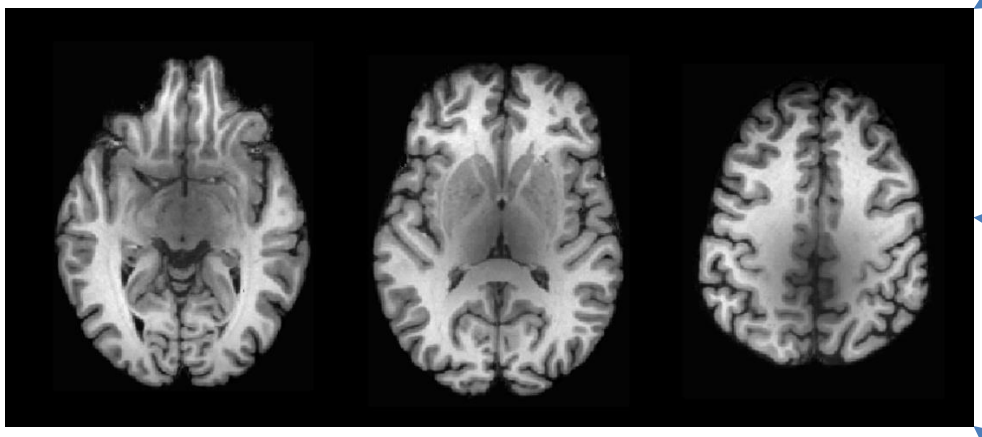
Interpreting morphological differences



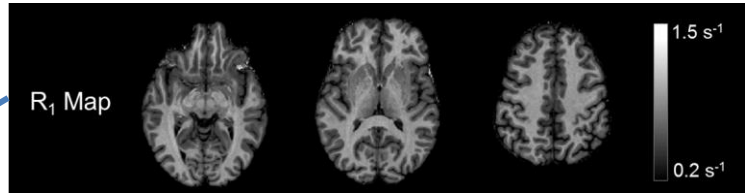
Helms et al., https://doi.org/10.1016/j.neuroimage.2009.03.053

Interpreting morphological differences

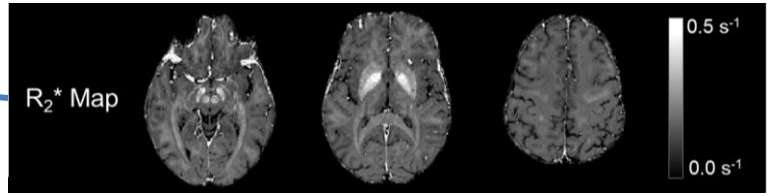
Signal Intensity = f (sequence parameters, scanner hardware, physical MRI parameters)



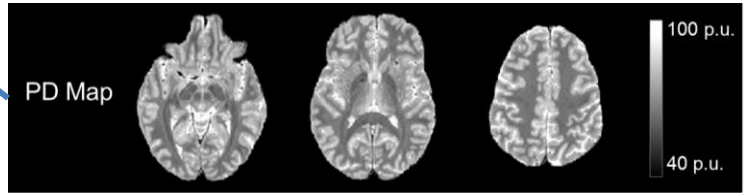
Longitudinal Relaxation Rate



Effective Transverse Relaxation Rate



Proton Density

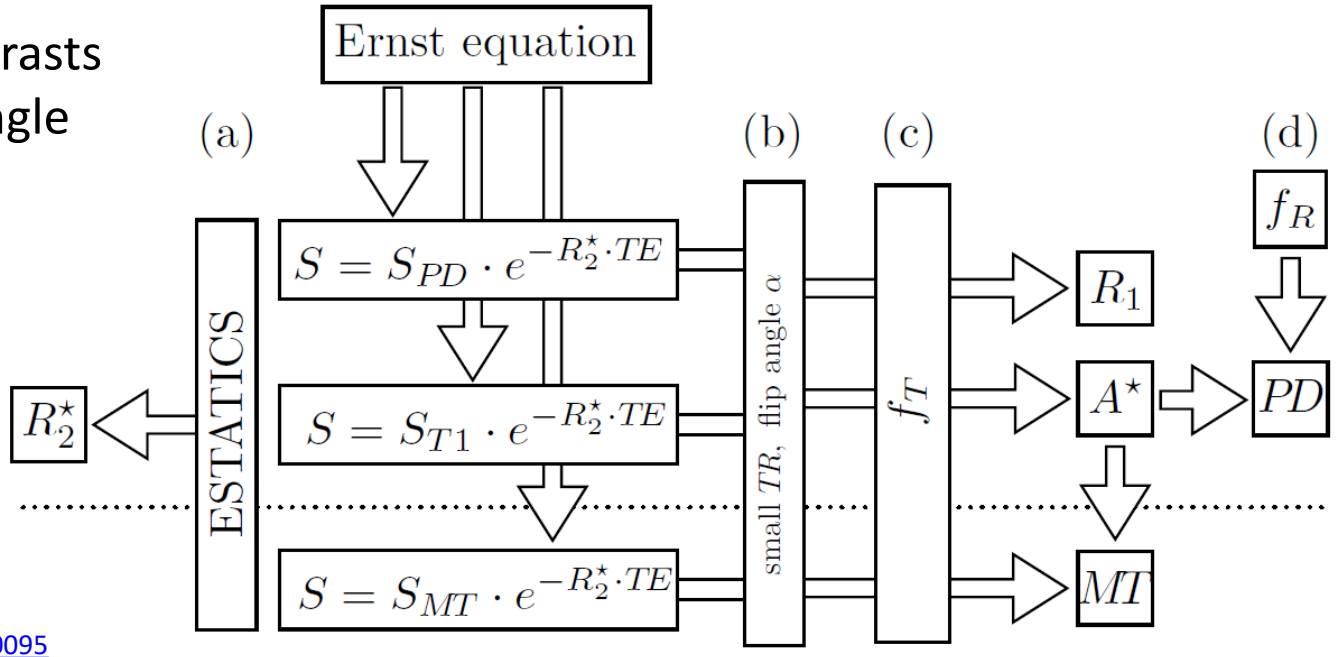


$\Rightarrow$ quantitative MRI

Multi-Parameter Mapping (MPM) Protocol

Whole-brain mapping of physical tissue properties:

- Fieldmaps (B_0/B_1^+/B_1^-)
- FLASH volumes
  - T1, PD, MT contrasts
  - Low/high flip angle
  - Multi TE
- Ernst equation



Weiskopf *et al.*,
https://dx.doi.org/10.3389%2Ffnins.2013.00095

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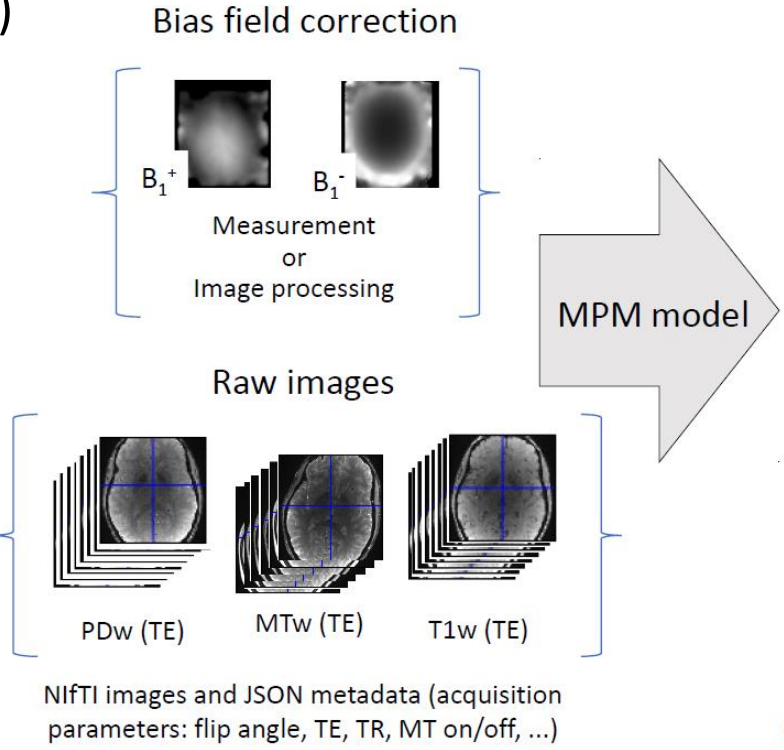
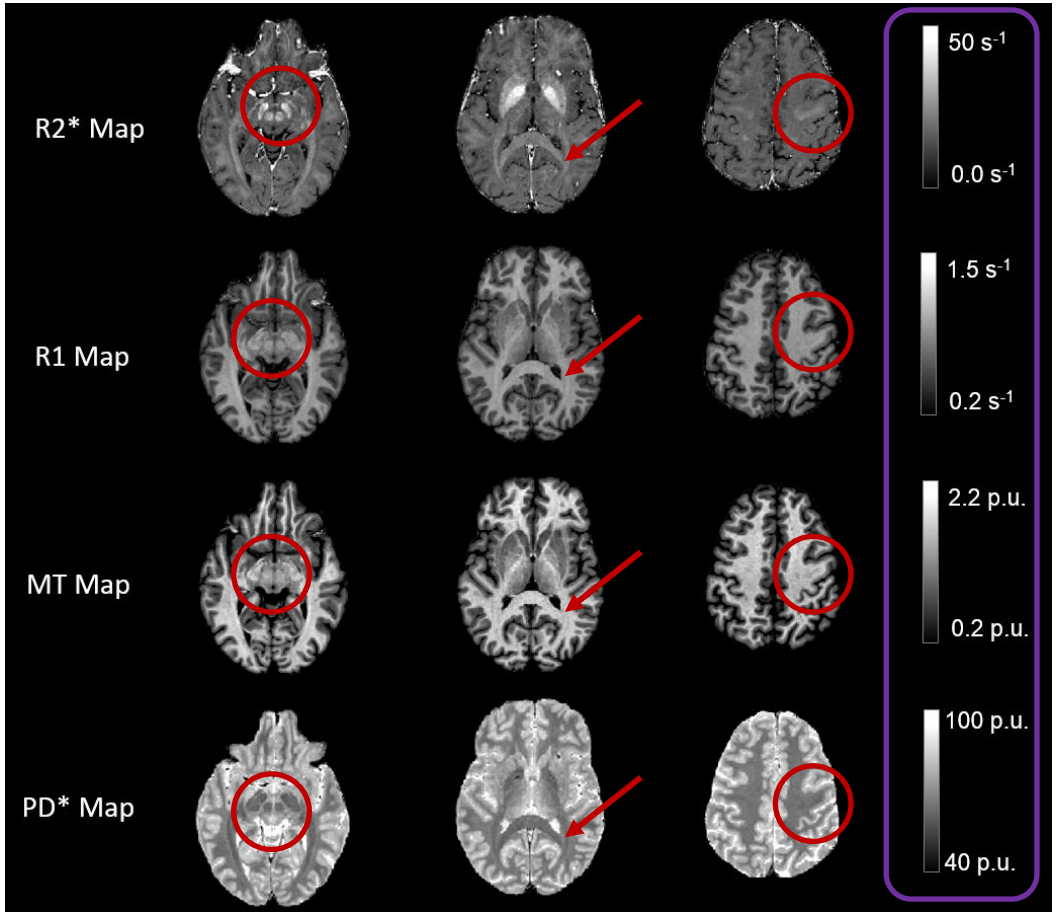


NIfTI images and JSON metadata (acquisition parameters: flip angle, TE, TR, MT on/off, ...)

NIfTI images and JSON metadata (processing parameters & description)

Weiskopf *et al.*,
https://dx.doi.org/10.3389%2Ffnins.2013.00095

MPM Protocol results

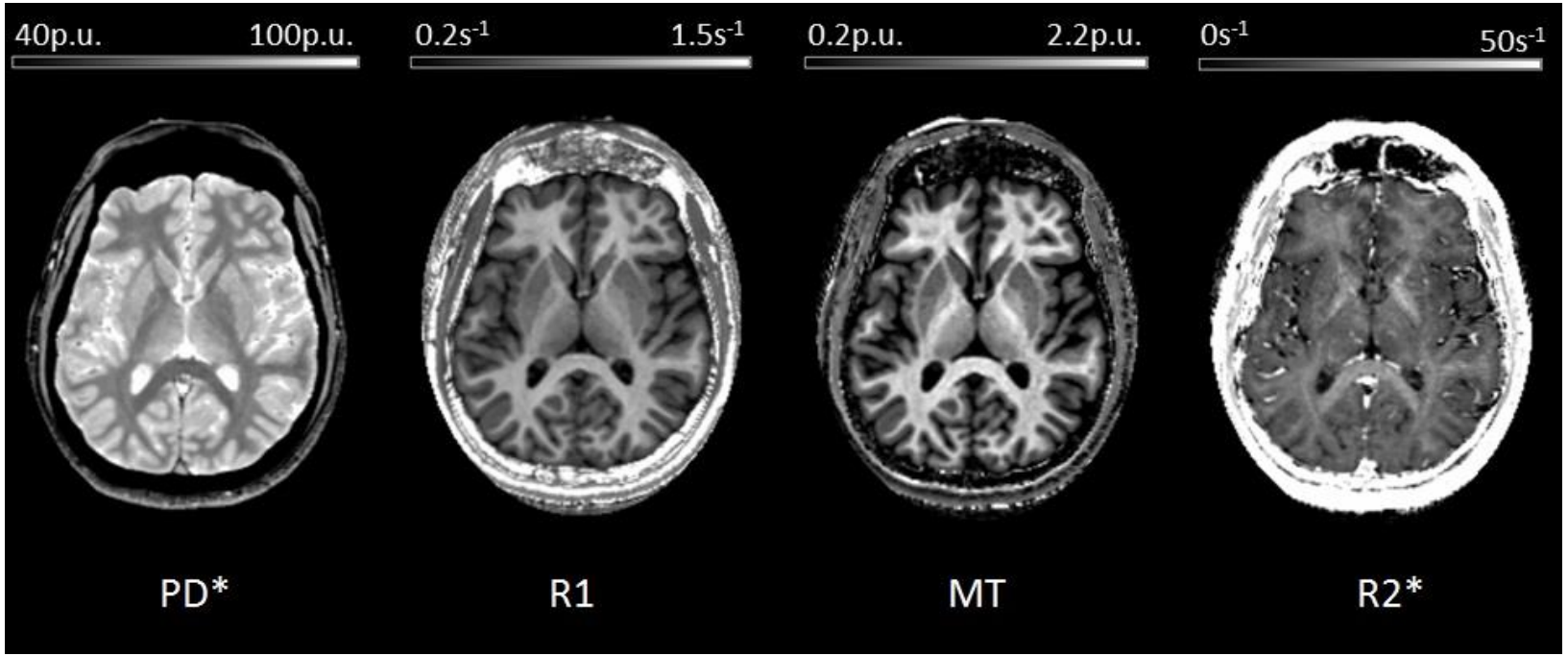


Four quantitative MRI (qMRI) parameters

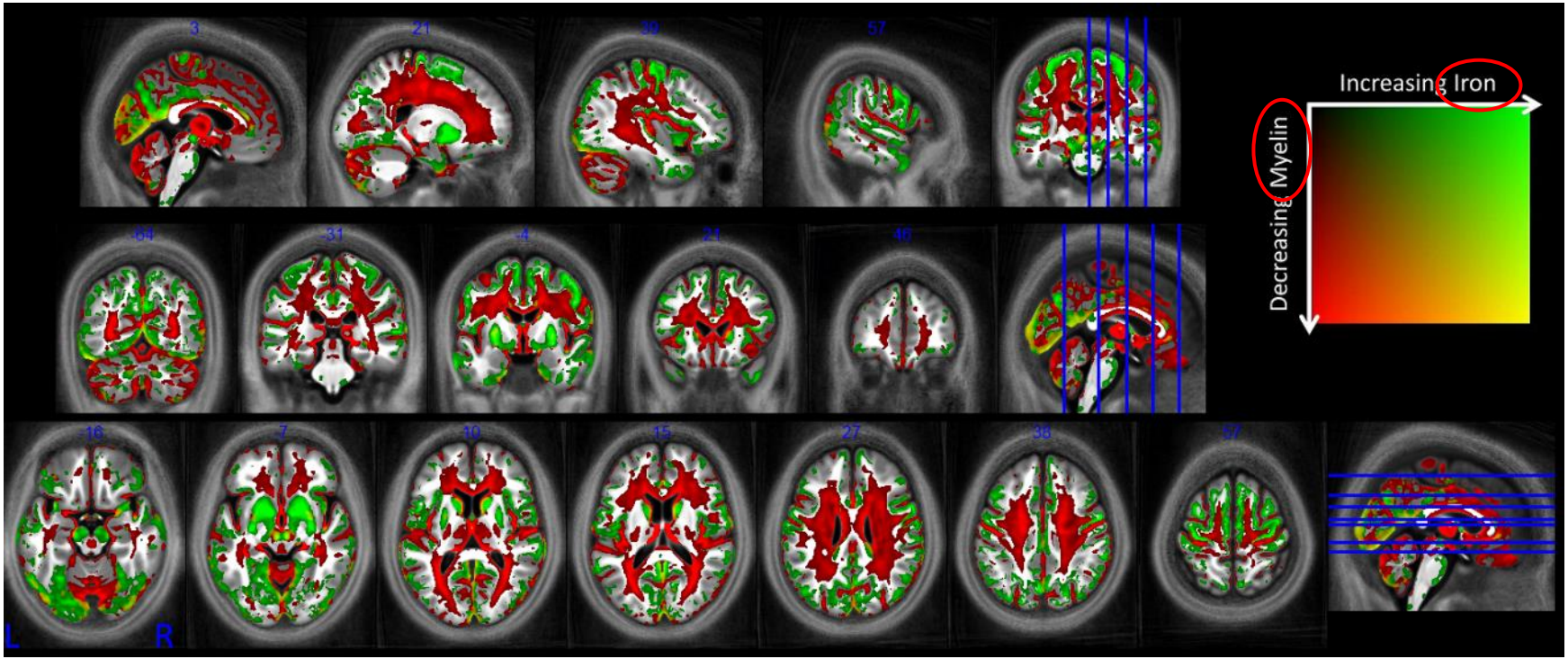
- Down to 800µm isotropic resolution with whole brain coverage
- Includes calibration for transmit and receive fields
- Less than 30 minutes scanning at 3T

qMRI interpretation

Water Content	Water Content; Macromolecules, e.g. myelin; Iron	Macromolecules e.g. myelin	Iron



Inter-individual differences: Aging



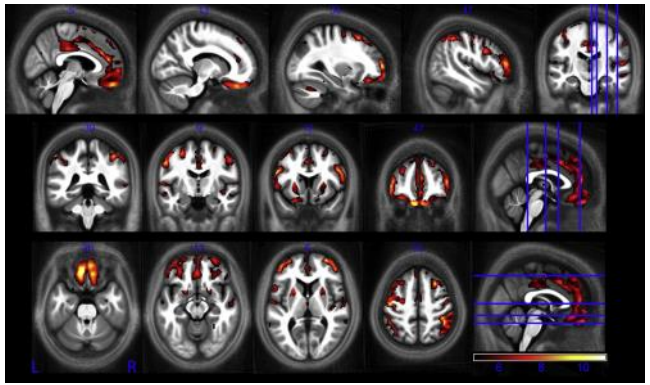
Broad age-related effects ($p<0.001$ uncorrected, for display purpose only)

Callaghan *et al.*, https://doi.org/10.1016/j.neurobiolaging.2014.02.008

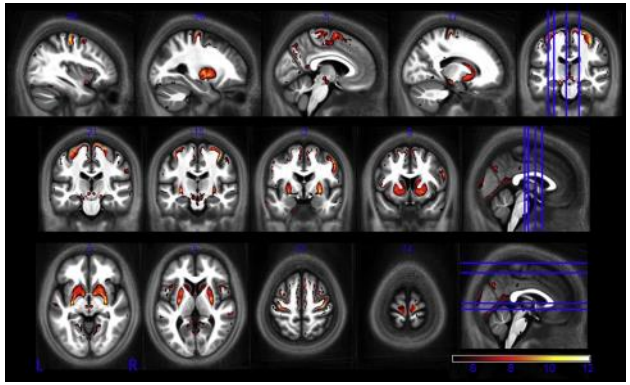
Inter-individual differences: Aging

Age-related effects (p<0.05 FWE corrected) per map

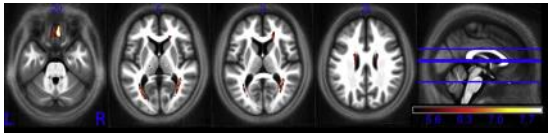
GM atrophy



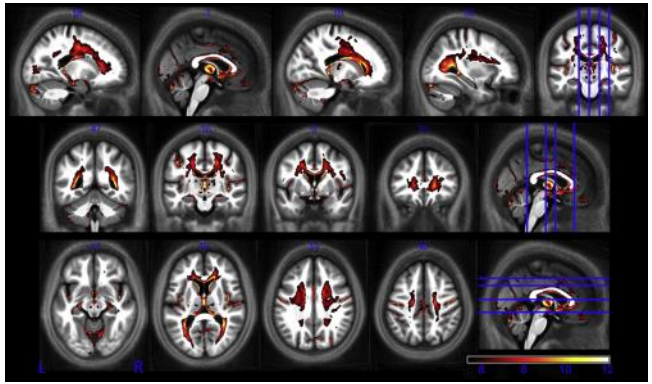
R2* increase



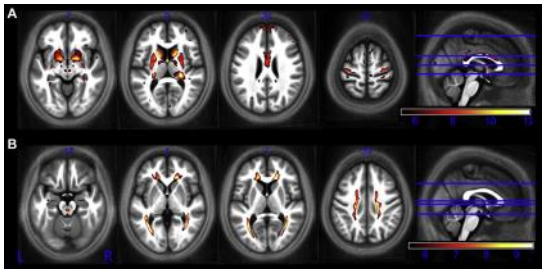
R2* decrease



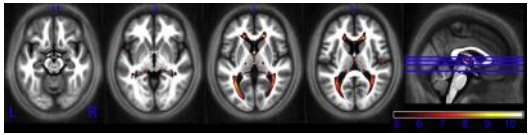
MT_{sat} decrease increase



PD decrease (A) and increase (B)

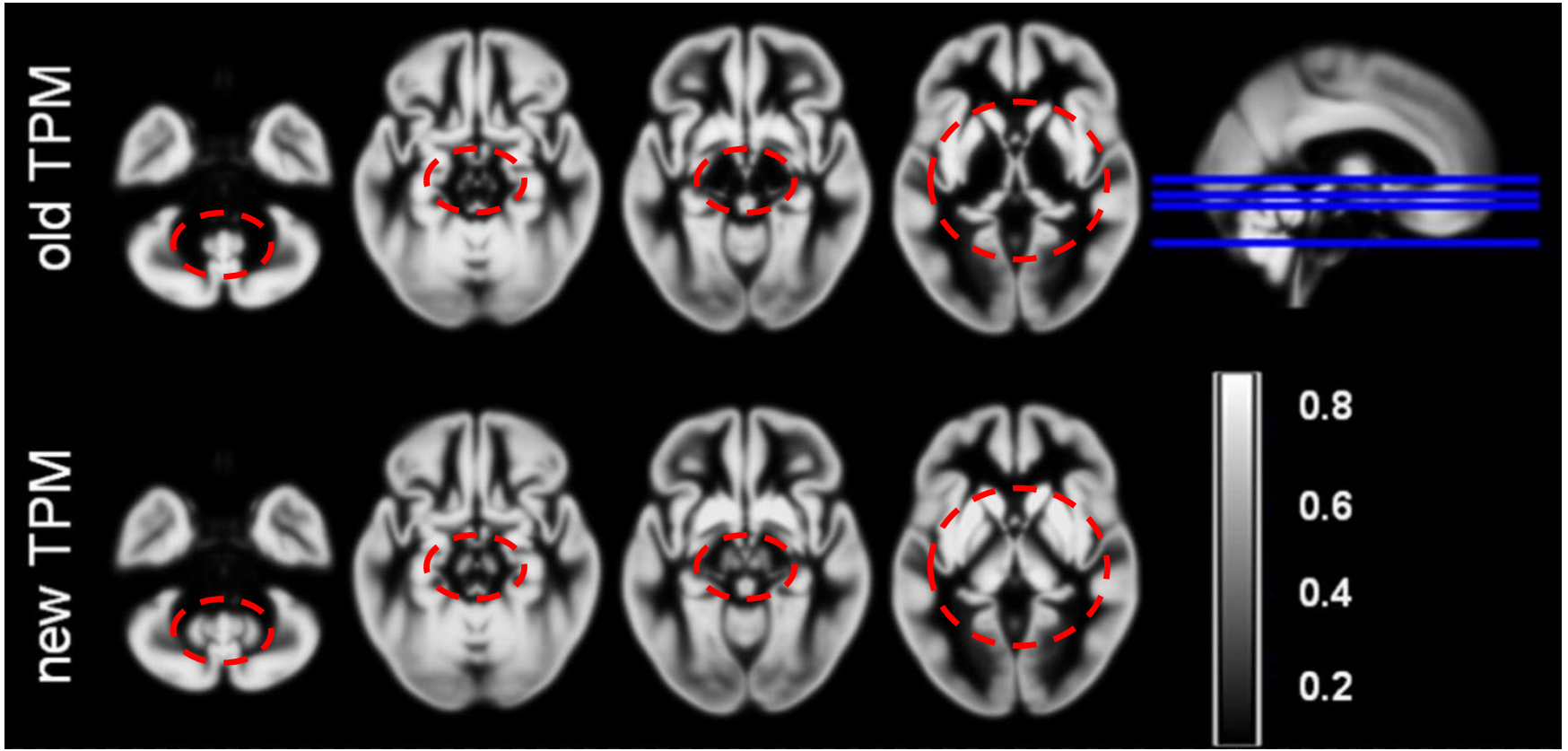


R1 decrease



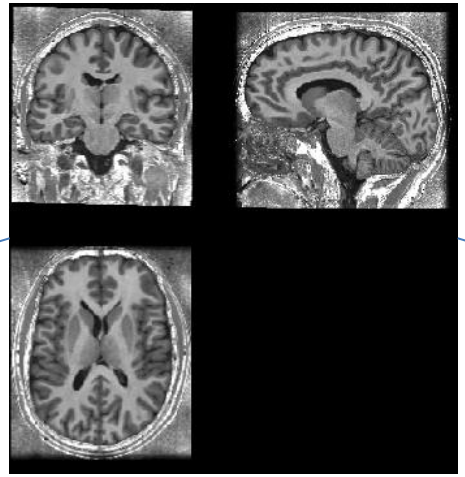
Callaghan *et al.*, https://doi.org/10.1016/j.neurobiolaging.2014.02.008

Segmentation issue: tissue probability maps



Lorio *et al.*, https://doi.org/10.1016/j.neuroimage.2016.01.062

VBQ: warping & tissue-weighted smoothing



Subject Space

GM in MNI Space

Using GM Probability

WM in MNI Space

Using WM Probability

$$\widehat{s_{1j}} = \frac{g * (w_j s_{1j})}{g * w_j} \frac{m_{TPM}}{m_j}$$

w_j = $J_{\Phi j} t_{\Phi j}$

= modulated warped posterior probability tissue map.

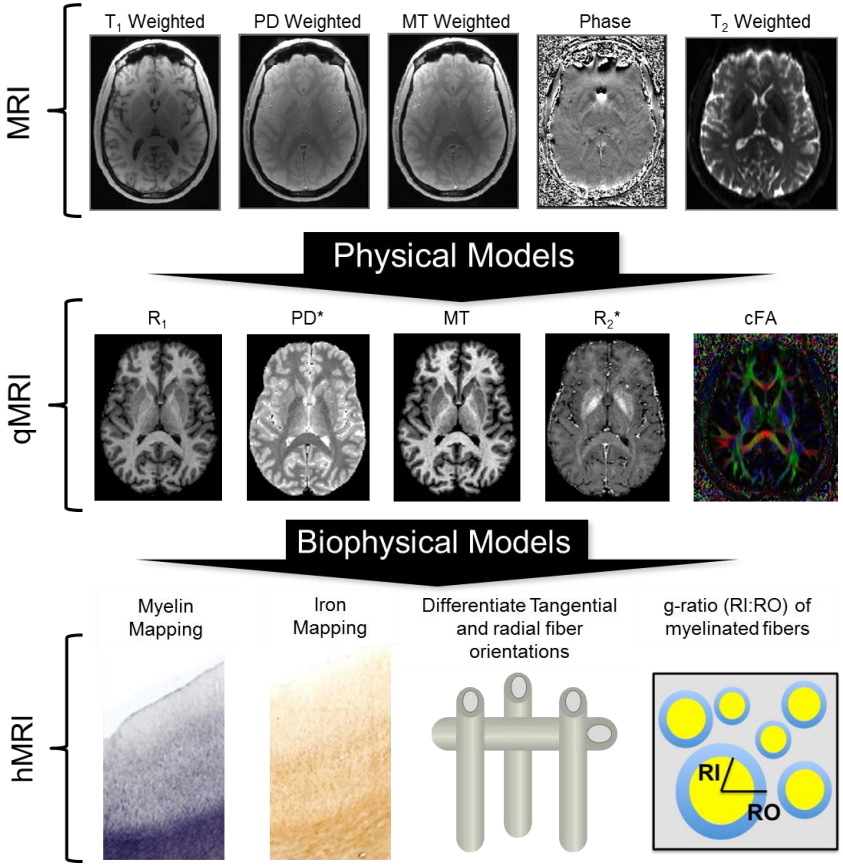
Draganski *et al.*, https://doi.org/10.1016/j.neuroimage.2011.01.052

Conclusions

- Morphometry still useful but…
- qMRI biomarkers
  - enhance specificity
  - disentangle effects via multi-modal quantification
  - reproducible across scanner
- getting closer to *in vivo* histology using MRI
  - follow tissue changes w/o (or before…) volume changes
  - (explore structure/function relationships)

Weiskopf *et al.*, https://doi.org/10.3389/fnins.2013.00095

In vivo histology using MRI (hMRI)



Begin by getting quantitative maps of specific parameters

The ultimate target is biological mapping

Weiskopf *et al.*, https://doi.org/10.1097/WCO.0000000000000222

Perspectives

- Improve MRI acquisition sequence:
  speed, SNR, resolution, different scanners,…
- Improve image reconstruction & processing:
  noisy voxels, automatization, data & meta-data organization (BIDS),…
- Linking to neuro-biological tissue properties:
  combining with PET, clinical applications,…
- Need specific software tool:
  e.g. “hMRI toolbox” (SPM add-on) & qMRlab to create and process maps

Some qMRI references

- Deep GM segmentation, https://doi.org/10.1016/j.neuroimage.2009.03.053
- MPM protocol, https://dx.doi.org/10.3389%2Ffnins.2013.00095
- New tissue probability maps, https://doi.org/10.1016/j.neuroimage.2016.01.062
- Tissue-weighted smoothing, https://doi.org/10.1016/j.neuroimage.2011.01.052
- Ageing studies, https://doi.org/10.1016/j.neurobiolaging.2014.02.008
- Multi-centre study, https://doi.org/10.3389/fnins.2013.00095
- hMRI review, https://doi.org/10.1097/WCO.0000000000000222
- Toolboxes, http://hmri.info & https://www.opensourceimaging.org/project/qmrlab/
  - hMRI toolbox, https://doi.org/10.1016/j.neuroimage.2019.01.029
  - qMRlab toolbox, https://doi.org/10.1002/cmr.a.21357

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Thank you for your attention!

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