THE DIFFUSION TIME DEPENDENCE OF MAP-MRI PARAMETERS IN THE HUMAN BRAIN

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INTRODUCTION

- Neuronal cells exhibit **self-similarity** across multiple length scales[1]. Brownian motion in **fractal-like media** leads to **anomalous diffusion**[2]
- Mean apparent propagator (MAP)-MRI[3] measures **diffusion propagators** in the live human brain[4] at a fixed diffusion time, yielding estimates of mean-squared displacements (MSD) and return-to-origin probability (RTOP)
- Temporal scaling (TS)-dMRI[5] measures **anomalous diffusion** by quantifying the **diffusion time dependent scaling** of MSD and RTOP
- We measured **propagators** at **different diffusion times** and derived preliminary values of TS-dMRI parameters in the living brain

METHODS

- **Whole-brain MAP-MRI** in 7 healthy volunteers with two diffusion times[6] Δ=19ms (434 DWIs, b_{max}=6.0ms/μm²) and Δ=49ms (466 DWIs, b_{max} =17.8ms/μm²);
- For both scans δ=8ms; 2mm isotropic resolution; FOV=21.6cm; TE/TR=77/4000ms; SMS=2; GRAPPA=2;
- From the motion and distortion corrected[7] dMRIs at each Δ we estimated **MAP propagators** (order 6), and computed the propagator anisotropy (PA), non-gaussianity (NG), RTOP, and fiber orientation distribution functions (fODFs)
- We quantified the **statistical difference** between co-registered propagators at different Δ with the Jensen-Shannon Divergence (JSD)[8]
- From the temporal scaling relations of MSD and RTOP, we estimated **TS-dMRI parameters**: the random walk dimension d_w and spectral dimension d_s, as well as the fractal dimension d_f:

$$MSD \propto t^{\frac{2}{d_w}} \qquad RTOP \propto t^{-\frac{2}{d_s}} \qquad d_f = \frac{d_w d_s}{2}$$

- We quantified the **reproducibility of MAP and TS-dMRI parameters** in test-retest experiments

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RESULTS

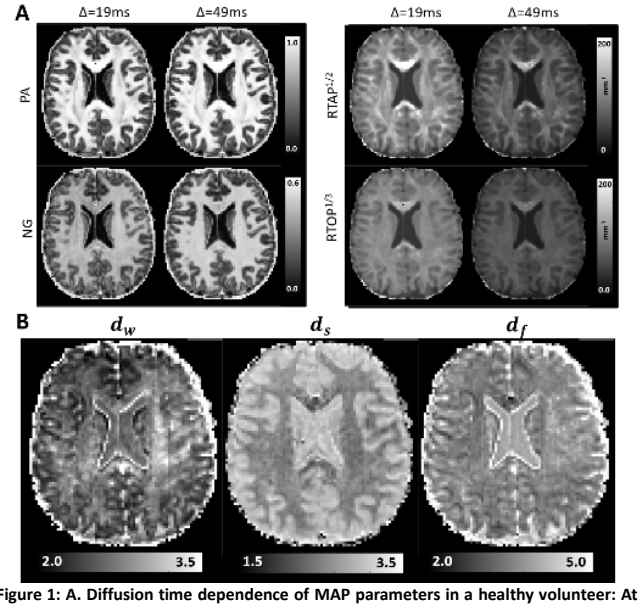

Figure 1: A. Diffusion time dependence of MAP parameters in a healthy volunteer: At larger Δ, RTAP, RTOP decrease throughout the brain, NG and PA increase in WM. B: Preliminary estimates of TS-dMRI parameters derived from the time-dependence of MAP propagators shows sub-diffusion throughout the brain d_w>2, largest GM/WM contrast in d_s, and a relatively flat d_f.

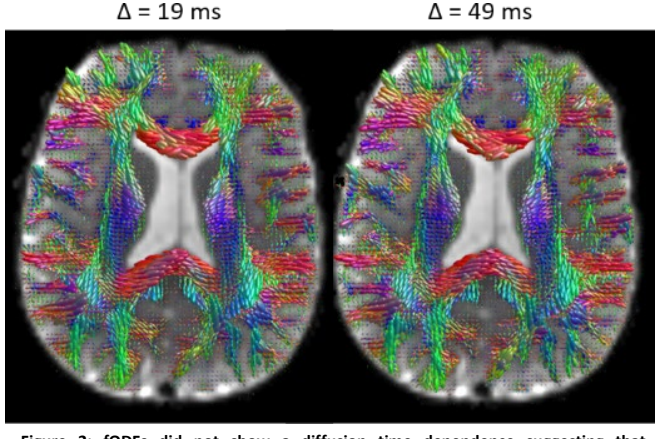

Figure 2: fODFs did not show a diffusion time dependence suggesting that applications such as fiber tractography are likely insensitive to Δ

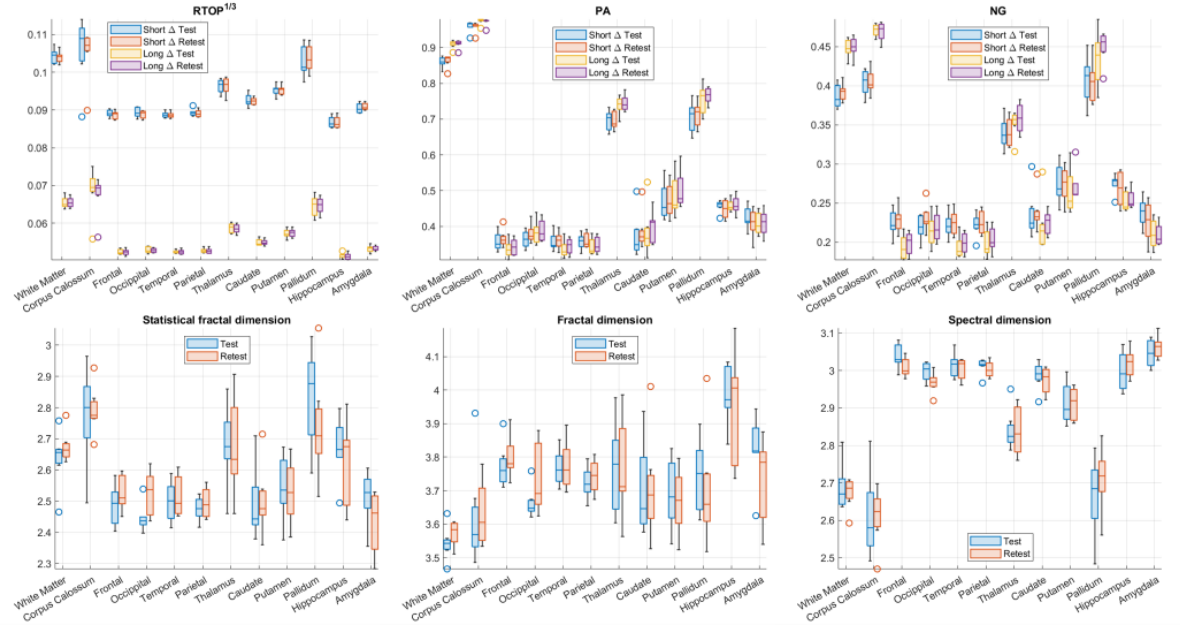

Figure 4: Anatomical variation of MAP-MRI at different diffusion times and TS-dMRI parameters measured in the cohort of 7 healthy volunteers. MAP parameters show good contrast between GM and WM, and some contrast in deep brain structures. All microstructural parameters show very good test-retest reproducibility.

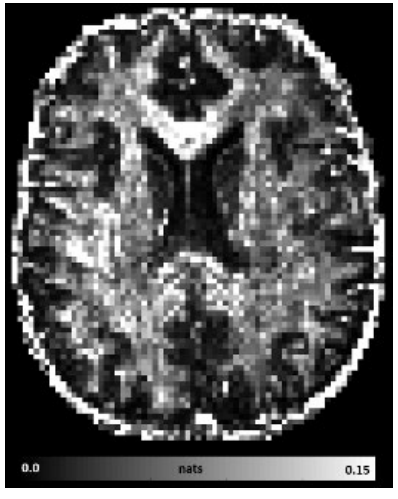

Figure 3: The largest JSD values between propagators measured with short and long Δ were found in compact WM, such as the corpus callosum, suggesting that microscopic restrictions are likely the major factor influencing the Δ-dependence

CONCLUSIONS

- **Zero-displacement probabilities** measured *in vivo* show *a* **strong diffusion time dependence** which must be taken into account when inferring morphological features[3,8] of tissues
- Despite good reproducibility, the **TS-dMRI parameters** estimated *in vivo* are **preliminary**
- Results from experiments sampling a **wider range of Δs** must be compared with other models of diffusion time dependence[9] in order to **validate anomalous diffusion** in living tissues
- The **temporal scaling** of diffusion propagators may yield **new tissue biomarkers** improving the diagnosis of brain injury and early onset of neurodegenerative diseases

References: 1. Smith et al., J. Neurosci Meth, **27**:173 (1989); 2. Gefen et al., Phys Rev Lett, **50**:77 (1983); 3. Özarslan et al. NIMG **78**, 16-32 (2013); 4. Avram et al. NIMG **127**, 422-434 (2016); 5. Özarslan et al., JMR **183:**315 (2006); 6. Huang et al., BSF **255**:1277 (2020); 7. Pierpaoli et al. ISMRM **18**, 1597 (2010); 8. Avram et al., ISMRM **27**:3470 (2019); 9. Avram and Basser, ISMRM **22**:3001 (2014); Novikov et al., MRM **79**:3172;