

Human cerebral aging is characterized by breakdown of microstructural restriction

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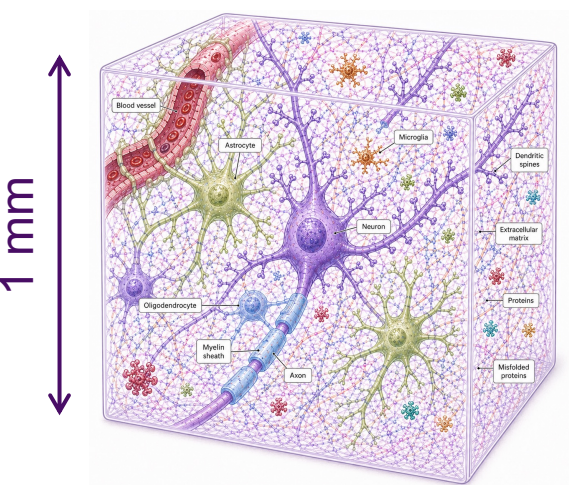
- MD-MRI detects age-related changes in diffusion, relaxation, and tissue heterogeneity.
- Normal aging is associated with breakdown of microstructural restriction.
- Diffusion frequency dependence is a sensitive marker of brain aging, likely reflecting expansion of the extracellular space

INTRODUCTION

❖ **MRI resolution is limited by voxel size**

➢ Microstructure heterogeneity in:

1. Cell density
2. Membrane properties
3. Extracellular content
4. Diffusion-relaxation behavior



→ Single average values cannot resolve intra-voxel complexity

❖ **Multidimensional MRI obtains information-rich distributions from each voxel**

Ten independent components

Mean ($E[X]$) and variance ($V[X]$) of:

- Isotropic diffusivity, D_{iso}
- Diffusion anisotropy, D_{Δ}^2
- Diffusion frequency dependence, $\Delta_{\omega/2\pi}$
- R_2 relaxation rate
- R_1 relaxation rate

METHODS

➢ Simultaneously fits the following parameters:

1. Isotropic diffusion (D_{iso})
2. Anisotropic diffusion (D_{Δ}^2)
3. Transverse relaxation rate (R_2)

→ **Multidimensional MRI is model-free and sensitive to cellular-scale features**

Group	Sample size	Sex (F/M)	Age (years)	
			Mean ± SD	Range
Young	17	9 / 8	25.6 ± 3.4	20-31
Middle	15	7 / 8	45.1 ± 6.2	32-57
Aged	14	7 / 7	67.3 ± 5.9	61-77
Total	46	23 / 23	47.3 ± 17.6	20-77

❖ **Participant Demographics**

- 46 healthy individuals recruited at the National Institutes of Health

RESULTS

❖ **Statistical Analysis**

- For each brain region and multidimensional MRI phenotype (P_r):
 $P_r = \beta_0 + \beta_{sex}Sex + \beta_{age}Age + \beta_{age^2}Age^2$
- False Discovery Rate correction: $pFDR < 0.05$

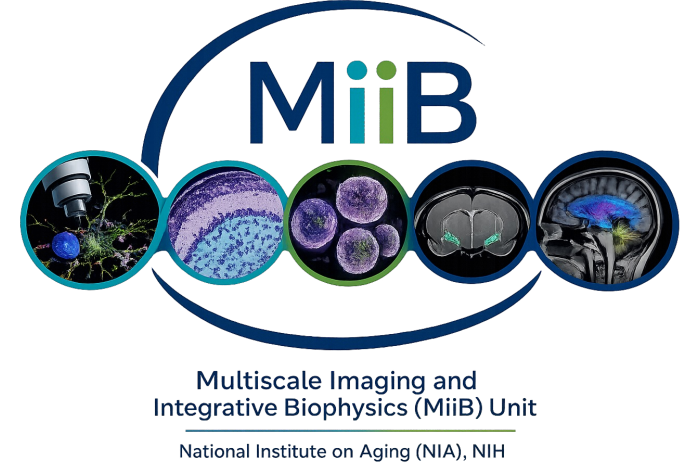
Figure 1. Representative MD-MRI parameter maps across young, middle-aged, and older adults. (A) Group-averaged maps of diffusion-relaxation metrics. (B) Percent differences between young and aged groups.

Figure 2. Age associations of multidimensional MRI parameters across cortical, deep gray matter, and white matter regions. (A) Standardized linear age effects (β_{age}). (B) Quadratic age effects (β_{age^2}) capturing nonlinear lifespan trajectories. (C) Representative regional trajectories with quadratic model fits and 95% confidence intervals. Asterisks indicate $P < 0.05$.

CONCLUSIONS

- MD-MRI captures age-related microstructural remodeling beyond conventional diffusion MRI.
- Reduction in microstructural restriction with age was observed across cortical, subcortical and white matter regions.
- Findings are consistent with expansion of extracellular space.

CONTACT



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