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Multivariate SPM analysis of quantitative MRIs: Widespread age-related differences revisited

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Introduction

Aging is along with alterations in the brain structure. Quantitative MR Imaging (qMRI) techniques provide in vivo neuroimaging biomarkers for myelination and iron content levels, which are sensitive to aging [1].

Here, we investigated the association of age with gray matter myelin and iron levels in a multivariate GLM model to see if we could achieve more convergent results than the conventional multiple univariate analysis.

Method and participants

| Participants	n=138
Age mean (s.d.) & range	46.64 (21) [19 75]
Male/Female %	35.5/64.5 %

- **Data z-transformation**. All map intensities are normalized based on the population mean and standard deviation.
- 4 univariate GLMs (**uGLM**) on quantitative maps. All uGLMs regress age & control for the effects of gender, total intracranial volume, and scanner.
- 1 multivariate GLM (**mGLM**) on all 4 quantitative maps, using the uGLM design matrices. This model can assess the concurrence of different changes at once.
- **Correcting for FWER** at $p<0.05$ for the mGLM F-test and $p<0.0125$ (=.05/4) for the uGLMs F-tests.
- The tests look for the **effect of age in gray matter tissues.**

Results

4 uGLMs: FWER corrected at $p<0.0125$

(A) PD (16,-33,9) mm

(B) MTsat (16,-33,9) mm

(C) R1 (16,-33,9) mm

(D) R2* (16,-33,9) mm
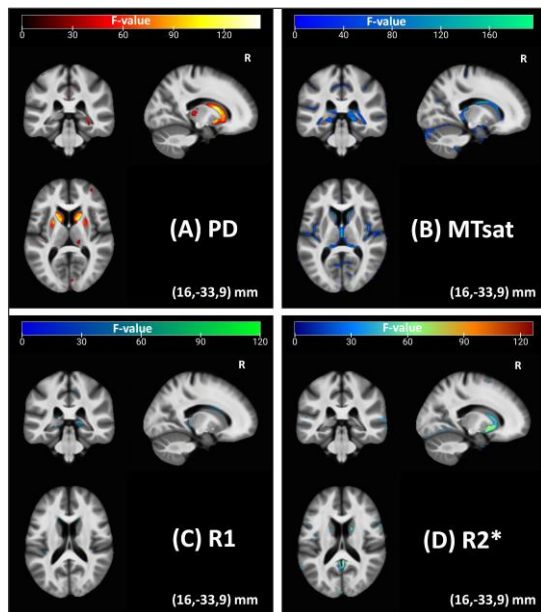
1 mGLM: FWER corrected at $p< 0.05$
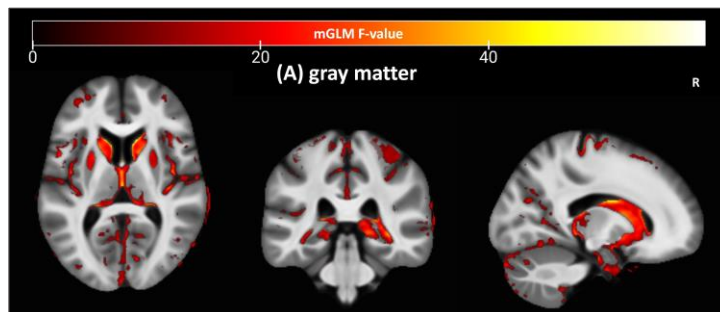
(A) gray matter

Gray matter: number of significant clusters and voxels

Map name	# clusters	Total # voxels
MTsat	265	50041
PD	212	22168
R1	142	6276
R2*	256	31993
4 GLMs united	570	**90323**
mGLM	564	**154098**

mGLM (FWER corrected at $p<0.05$) **vs. union of 4 uGLMs** (FWER corrected at $p<0.0125$)

L   R

■ mGLM only
■ union of 4 GLMs only
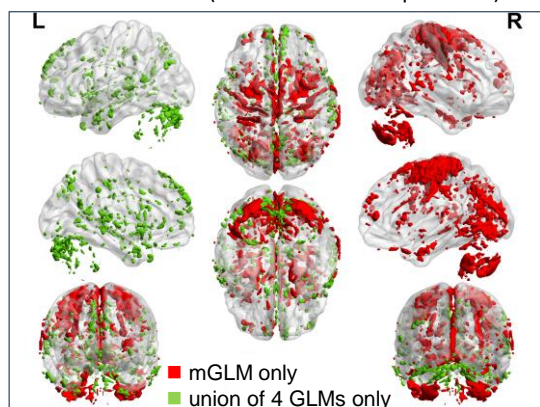
Discussion

- One mGLM is preferable to multiple uGLM analyses, as it better controls the risk of false positives.
- mGLM outperforms the uGLM models in gray matter accounting for the concurrence of microstructural changes in the brain.
- The mGLM, although less conservative, exhibited larger sensitivity to the changes associated with all maps compared to the uGLMs.
- We observe bilateral age-related changes in the supplementary motor area, frontal cortex, hippocampus, amygdala, occipital cortex, and cerebellum, indicating the co-occurrence of alterations in MTsat, R2*, and PD maps, associated with myelin, iron, and free water content in the brain.

References

1. Callaghan et al., 2014. doi: 10.1016/j.neurobiolaging.2014.02.008
2. Gyger et al., 2021. doi: 10.1016/j.neuroimage.2021.117895
3. Draganski et al., 2011. doi: 10.1016/j.neuroimage.2011.01.052