In-vivo dynamical effects of structural white matter disconnections

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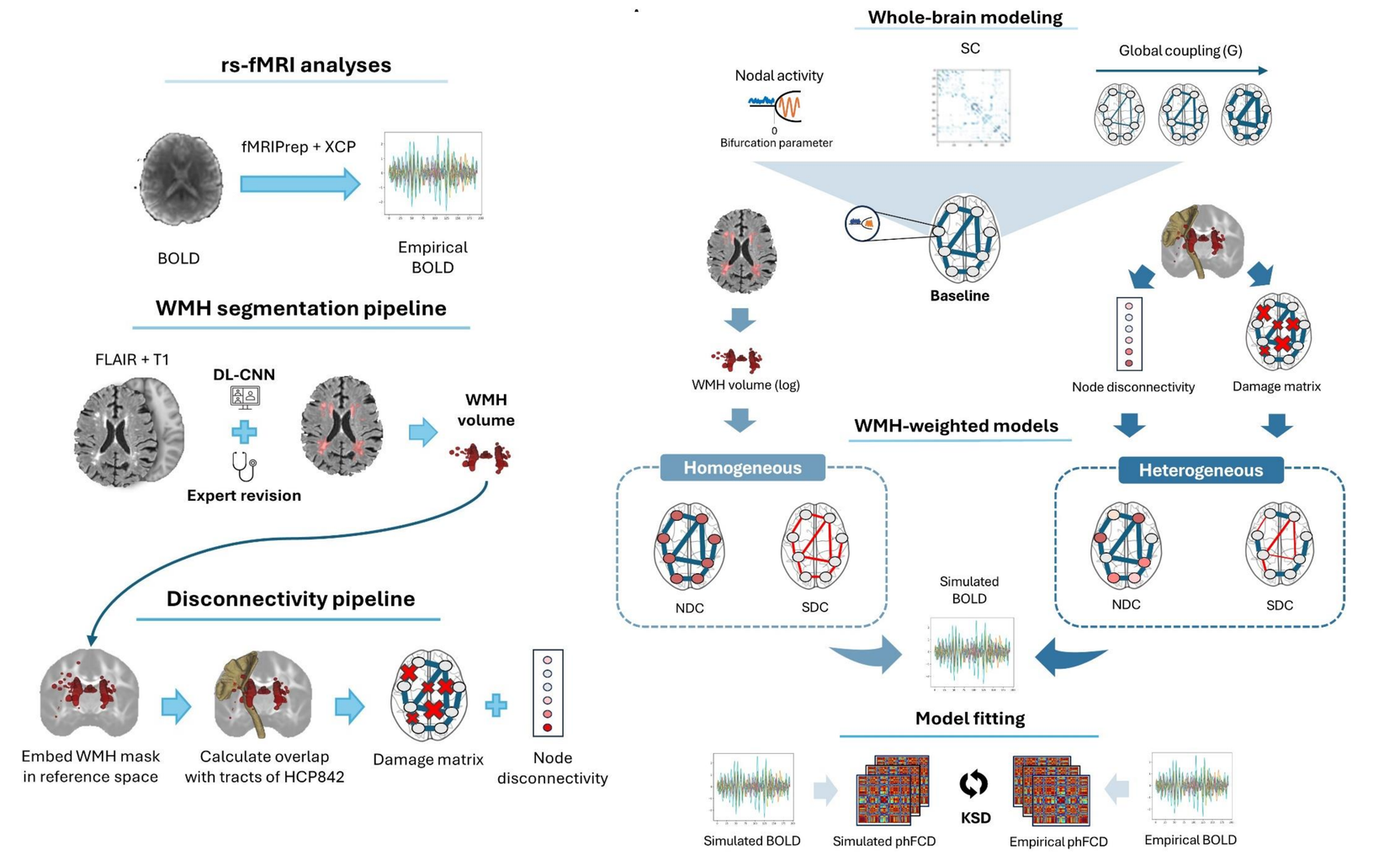
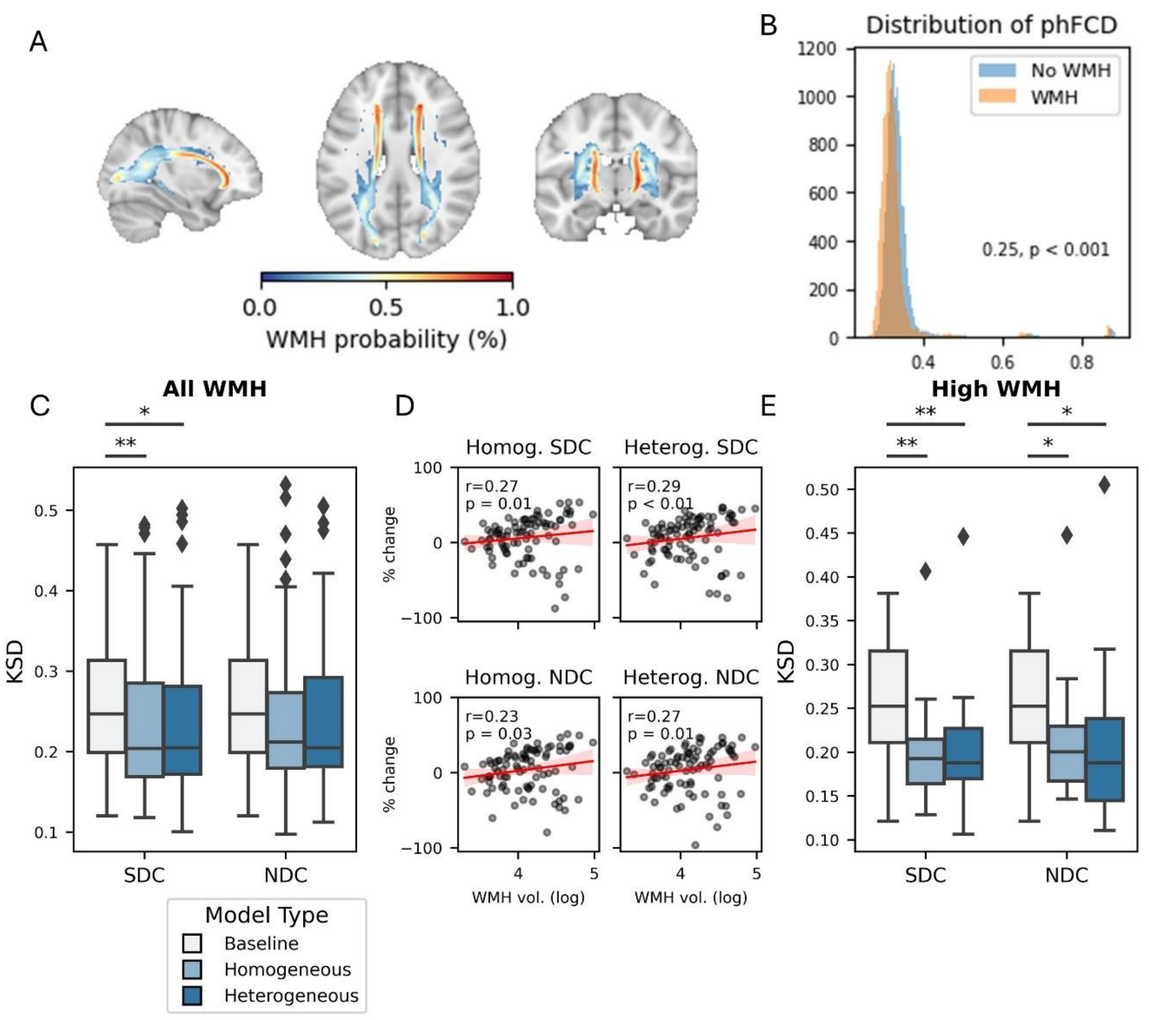
Background

White matter (WM) tracts shape the brain's dynamical activity and their damage (e.g., white matter hyperintensities, WMH) yields relevant functional alterations, ultimately leading to cognitive symptoms. The mechanisms linking the structural damage caused by WMH to the arising alterations of brain dynamics is currently unknown. To estimate the impact of WMH on brain dynamics, we combine neural-mass whole-brain modeling with a virtual-lesioning (disconnectome) approach informed by empirical data. We account for the heterogeneous effects of WMH either on inter-regional communication (i.e., edges) or on dynamics (i.e. nodes) and create models of their local versus global, and edge versus nodal effects using a large fMRI dataset comprising individuals with varying degrees of WMH.

Methods: workflow



Results (I)



(A) Maximum intensity projections along the sagittal (left), axial (middle) and coronal (right) planes of WMH probability maps.

(B) Group-averaged phase functional connectivity dynamics (phFCD) in the groups without (blue) and with (orange) relevant WMH.

(C) Model comparisons between the baseline (white) and the homogeneous (light blue) and heterogeneous models (dark blue).

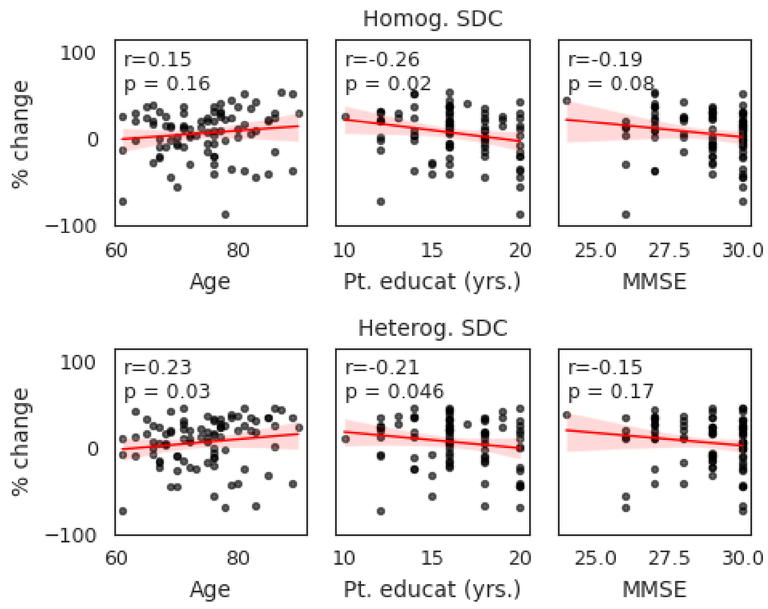
(D) Correlations between WMH volume (log-transformed, along the x axes) and the percentage of improvement in model fit compared to the baseline model

(E) Same as in (C) only in the group with the highest Fazekas score of 3.

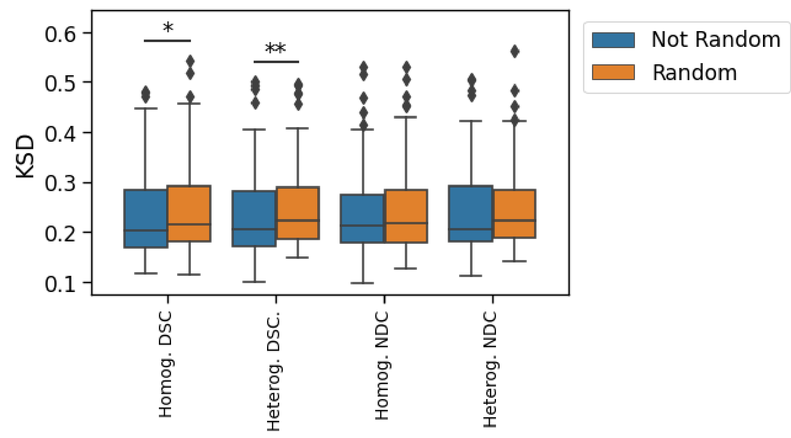
SDC : structural dysconnectivity
NDC: node disconnectivity

*: 0.01 < p < 0.05, **: 0.001 < p <= 0.01.

Results (II)



Scatterplots depicting the correlation between demographics factors (age, years of patient education and mini-mental status examination (MMSE), and the percentage improvement in model performance of the considered model compared to the baseline model. The first row shows the results for the homogeneous structural disconnectivity model (SDC), while the second row shows the results for the heterogeneous SDC



Boxplots comparing the random and non-random versioni of WMH-weighted models. Homogeneous and heterogeneous SDC models goodness of fit to the empirical data is significantly better for the non-random version compared to the random one.

Conclusions

We provided generative models linking the structural damage caused by WMH to alterations in brain dynamics. These models might be used to evaluate the detrimental effects of WMH on brain dynamics in a subject-specific manner. Furthermore, we validate the use of whole-brain modeling for hypothesis-testing of structure-function relationships in diseased states characterized by empirical disconnections.

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