Healthy white matter predicts up-regulation of functional brain activity in premanifest Huntington’s disease

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Background: Organizational characteristics of healthy brain-networks predict the topological distribution of pathology in neurodegenerative diseases, such as Huntington’s Disease (HD) and Alzheimer’s disease (AD). However the extent to which such structural characteristics of white matter might impact on brain activity in pre-clinical neurodegeneration is unknown. Understanding this relationship will help identify the earliest brain changes occurring prior to irreversible structural loss.

Methods: Using diffusion tractography and resting state fMRI to characterize white matter organization and functional connectivity, we investigate whether characteristic patterns of white matter organization derived from the healthy human brain shape the changes in functional connectivity in premanifest HD, even years before clinical presentation.

Results: We found that white matter organization in the brains of healthy controls strongly predicted how functional connectivity changed in premanifest HD. Specifically, regions with low white matter connectivity showed distinct increases in functional connectivity in premanifest HD.

Conclusions: Our findings thus reveal that large-scale organizational principles of white matter networks underlie functional connectivity change in premanifest HD.