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Thursday

Structure-function decoupling as a marker of neurodegeneration in C9orf72 expansion carriers

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State of the art
Biomarkers are critically lacking for the monitoring of disease progression and strategizing early therapeutic interventions for C9orf72 repeat expansions. Neurodegeneration is known to affect the dependence of functional activity on underlying structural network (structure-function coupling). We hypothesize structure-function decoupling is a marker of neurodegeneration in C9orf72.

Methodology
We evaluated a structure-function coupling index through graph frequency analysis of functional activity from resting-state fMRI as graph data and diffusion connectome from dMRI as the graph in a cohort of asymptomatic C9orf72 (AC9; N=11), symptomatic C9orf72 (SC9; N=10), and healthy controls (HC; N=6) from the Human Connectome Project-Frontotemporal Degeneration (FTD) study. We quantified the structure-function coupling index at every node in an atlas parcellation and residualized for age, with a higher structure-function coupling index representing more coherence between structure and function. We relate structure-function coupling to plasma neurofilament light chain (NfL) measured using Quanterix immunoassay.

Results
ANOVA revealed that structure-function coupling was lower for SC9 than HC, and intermediate for AC9 relative to SC9 and HC, in bilateral ventromedial prefrontal cortex, left anterior cingulate, and right insula and inferior temporal regions. Plasma NfL was negatively correlated with structure-function coupling indices for the combined AC9 and SC9 cohort in right ventromedial prefrontal and left dorsal prefrontal cortex.

Conclusion
We observed evidence of structure-function decoupling in anatomically plausible regions for SC9 relative to HC and negative correlation with NfL in the combined AC9 and SC9 cohort. Therefore, loss of structure-function coupling may be a plausible feature of C9orf72 neurodegeneration.

Conflicts of interest

No relevant conflicts of interest relevant to this research.