Comment: Network disruption as a common framework for factors contributing to dementia

There is mounting evidence that large-scale functional brain networks are fundamental to the pathophysiology of dementing illnesses.[1] Functional networks require intact white matter, and small vessel disease (SVD) may disrupt this infrastructure. Tuladhar et al.[2] conducted an analysis of imaging biomarkers as predictors of all-cause dementia in a prospective hospital-based cohort of patients with presumed evidence of SVD. The imaging biomarkers included white matter network–based graph theoretical metrics (e.g., global network efficiency), white matter volume, gray matter volume, hippocampal volume, manually segmented white matter hyperintensity volume, and presence/absence of lacunes and microbleeds.

The authors found that measures of SVD were correlated with network measures indicating shared information between these metrics. However, they demonstrate that among the imaging biomarkers studied, hippocampal volume and global network efficiency were the only imaging predictors of all-cause dementia in their cohort. This result suggests that one way by which factors associated with SVD contribute to dementing pathophysiology is via their effects on large-scale networks.

While diffusion MRI-based tractography may not be able to reproduce true structural connectivity faithfully,[3] the current study demonstrates that this technique can create biologically relevant models of white matter networks that contain information that is absent in traditional markers of white matter integrity. A key piece of information that is lacking in traditional measures of white matter integrity is the importance of lesion location to global network function. For example, strategic insults located in pathways connecting hubs of high importance will be modeled by traditional biomarkers as having the same effect as lesions of little importance to global network communication. However, measures sensitive to these lesions that can be used to generate network models will be sensitive to strategic differences in lesion location.

This study supports the utility of using network measures as biomarkers of pathophysiologic processes related to the development of dementia.

1. Jones DT, Knopman DS, Gunter JL, et al. Cascading network failure across the Alzheimer's disease spectrum. Brain Epub 2015 Nov 19.
2. Tuladhar AM, van Uden IWM, Rutten-Jacobs LC, et al. Structural network efficiency predicts conversion to dementia. Neurology 2016;86:xx–xx.
3. Reveley C, Seth AK, Pierpaoli C, et al. Superficial white matter fiber systems impede detection of long-range cortical connections in diffusion MR tractography. Proc Natl Acad Sci USA 2015;112:E2820–E2828.

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