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David T. Jones^{1,2*}, Jonathan Graff-Radford¹, Val J. Lowe², Heather J. Wiste³, Jeffrey L. Gunter^{2,4}, Matthew L. Senjem^{2,4}, Hugo Botha¹, Kejal Kantarci², Bradley F. Boeve¹, David S. Knopman¹, Ronald C. Petersen¹, Clifford R. Jack, Jr.²

Affiliations:

¹Department of Neurology, ²Department of Radiology, ³Department of Health Sciences Research,

⁴Department of Information Technology, Mayo Clinic, Rochester, MN, USA.

Contact:

*Correspondence to: David T. Jones, Mayo Clinic, 200 First Street S.W., Rochester, MN 55905

jones.david@mayo.edu

Running Title:

Tau, amyloid, and networks

Abstract:

Functionally related brain regions are selectively vulnerable to Alzheimer's disease pathophysiology. However, molecular markers of this pathophysiology (i.e., beta-amyloid and tau aggregates) have discrepant spatial and temporal patterns of progression within these selectively vulnerable brain regions. Existing reductionist pathophysiologic models cannot account for these large-scale spatiotemporal inconsistencies. Within the framework of the recently proposed cascading network failure model of Alzheimer's disease, however, these large-scale patterns are to be expected. This model postulates the following: 1) a tau-associated, circumscribed network disruption occurs in brain regions specific to a given phenotype in clinically normal individuals; 2) this disruption can trigger phenotype independent, stereotypic, and amyloid-associated compensatory brain network changes indexed by

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