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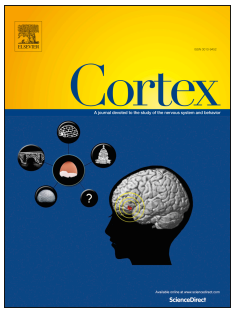

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Tau, Amyloid, and Cascading Network Failure across the Alzheimer's disease Spectrum

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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