On the intra-brain Propagation of Pathologic Functional Signals in Neurodegeneration

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Abstract:

Mechanisms underlying neurodegenerative progression are still poorly characterized from an integrative perspective. Models that define neurodegenerative pathogenesis are based on limited data that do not cover all biological factors influencing disease progression. This traditional lack of quantitative integrative models is a crucial obstacle towards the development of effective disease therapeutic agents. We will present our recent work analyzing spatiotemporal alterations in intra-brain amyloid-ß deposition and functional activity, which an emphasis on how associated pathologic effects propagate across brain networks and which specific pathologic factors modulate/promote such propagation. For this, we analyzed multi-modal data for about 900 healthy and diseased subjects from Alzheimer's Disease Neuroimaging Initiative (ADNI; http://adni.loni.usc.edu/), including resting-fMRI, amyloid PET and structural MRI, as well as cognitive/clinical and genetic measurements. We used and epidemic spreading model (Iturria-Medina et al. 2014) to characterize the concurrent propagation of amyloid and aberrant functional signals, through the brain's structural connectome. Our results highlight the crucial role of brain connectivity on neurodegenerative progression as well as the key importance of considering multi-factorial pathologic interactions on the study of neurodegenerative disorders. These results might provide a turning point for the development of preventive therapeutic interventions, whereas the introduced model may be an accurate descriptor of drugs responses, predicting multi-factorial deviations from disease trajectories. We will also emphasize current limitations and challenges associated with the modeling of neurodegeneration.