Understanding the Influence of Amyloid-Beta and Tau in Alzheimer's Disease through Whole-Brain Dynamics

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Introduction:
Alzheimer's disease (AD) affects brain structure and function along its evolution, but brain network dynamic changes remain largely unknown.

Methods:
To understand how AD shapes brain activity, we investigated the spatiotemporal dynamics and resting state functional networks using the intrinsic ignition framework [Deco and Kringelbach 2017], which characterizes how an area transmits neuronal activity to others, resulting in different degrees of integration [Deco et al. 2017]. See Figure 1. Healthy participants, MCI, and AD patients were scanned using resting state fMRI [Stefanovski et al. 2021]. Mixed effects models were used to assess the impact of ABeta and tau, at the regional and whole-brain levels.

Results:
Dynamic complexity is progressively reduced, with Healthy participants showing higher metastability (i.e., a more complex dynamical regime over time) than observed in the other stages, while AD subjects showed the lowest. See Figure 2.

Discussion:
Our study provides further insight into how AD modulates brain network dynamics along its evolution, progressively disrupting the whole-brain and resting state network dynamics.

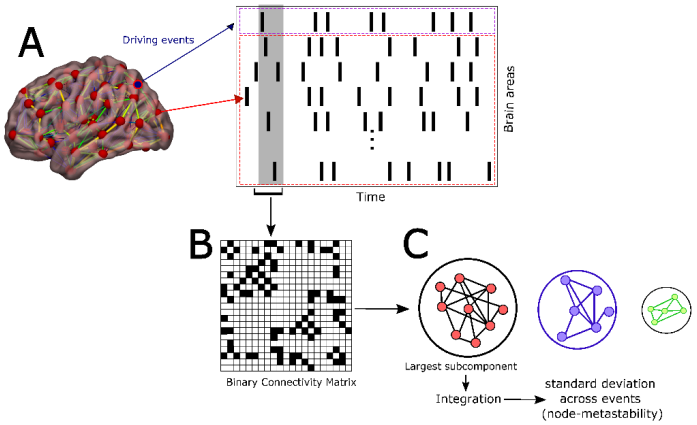

Figure 1: Intrinsic ignition Framework. (A) Events were captured applying a threshold method [43] (see purple area). For each event elicited (a gray area), the activity in the rest of the network was measured in the time window of 4TR (see red area). (B) A binarized matrix was obtained, representing the connectivity between brain areas where activity was simultaneous. (C) Applying the global integration measure [Deco et al. 2017], we obtained the largest subcomponent. Repeating the process for each driving event, we calculated the node-metastability computed as the standard deviation of the integration of each brain area over time.

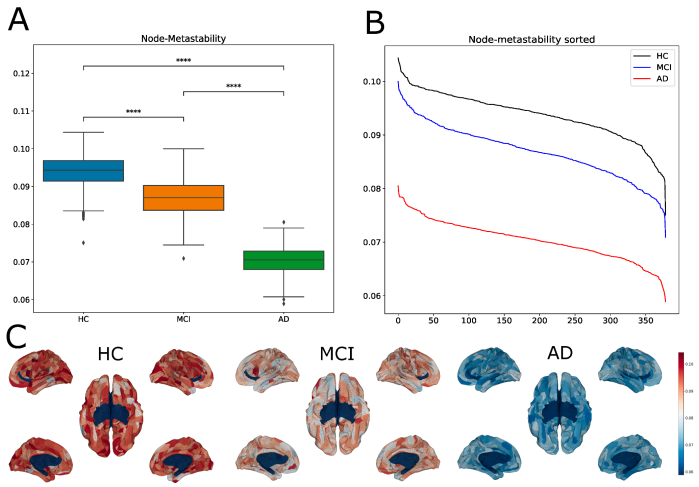

Figure 2: Dynamical complexity of Alzheimer's Disease stages. (A) Node-metastability. Healthy controls showed higher node-metastability values across the whole-brain network than the MCI and AD stages. (B) Hierarchy. The red area marks the ten regions showing the highest metastability values in each stage. For the Healthy controls, brain areas showing the highest values were primarily located in the visual, somatomotor, and dorsal attention networks. For the MCI stage, the brain areas belonged to the same networks, except that, besides the visual network, with a lower metastability. Finally, during the AD stage, they were located again in the visual, somatomotor, and dorsal attention networks, although with a severe decrease in metastability. (C) Brain renders represent the metastability values of the 379 areas for each disease stage. The dynamical complexity of the healthy controls across the whole-brain networks is more complex than the dynamical complexity of the other two stages.

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