Neurochemical and Pathological Drivers of Network Stability: Dopamine and Tau in Aging

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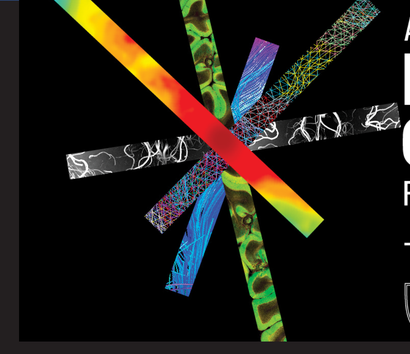

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Background

- Cognition depends on balancing segregated resting networks with selective task integration. [1–3]
- Rest-to-task network stability and network segregation quantify this balance and predict individual differences in cognition. [4–6]
- Aging is associated with reduced segregation (and emerging evidence for reduced stability), which are both linked to poorer cognitive outcomes. [7–10]
- Dopamine may stabilize task-relevant network states, but PET evidence linking dopamine to network stability/segregation is limited. [11–13]
- In amyloid-beta-positive older adults, tau is linked to disrupted reconfiguration and reduced segregation. [14,15]

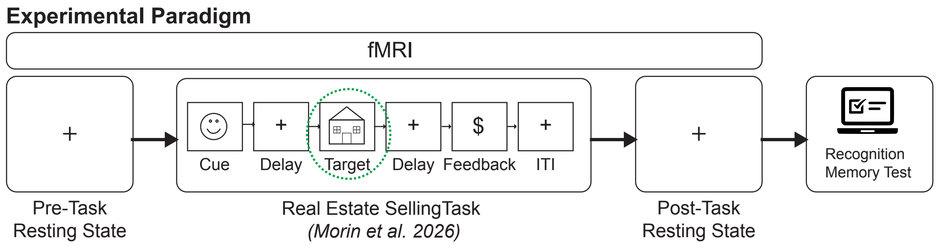
Research Questions:

- How does age affect network stability and segregation?
- Do dopamine PET measures (Catecholamine Synthesis Capacity) relate to network stability and segregation?
- Does Alzheimer's pathology affect functional network stability and segregation?

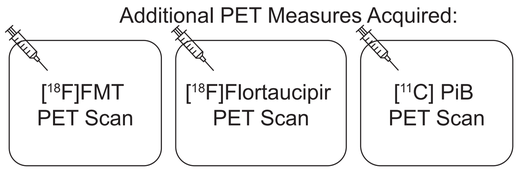
Methods

Participants: Healthy older adults (Age 60 - 80; n = 50) and young adults (Age 18 - 35; n = 30)

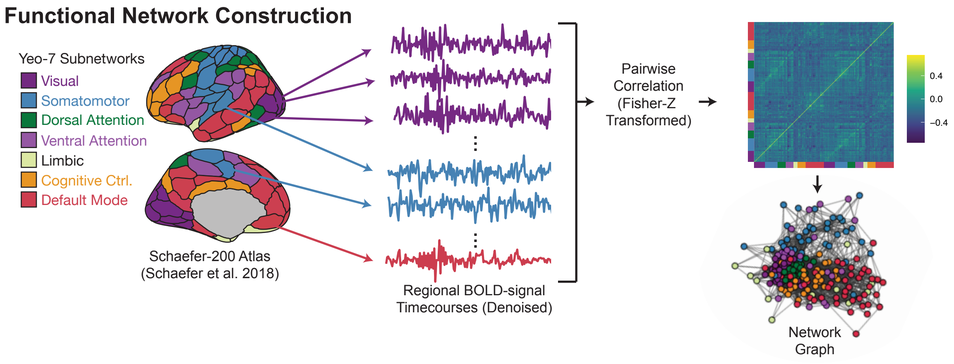
Experimental Paradigm



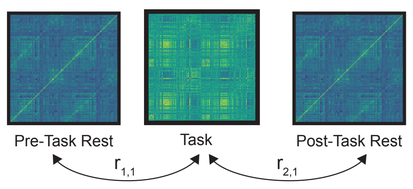
Additional PET Measures Acquired:



Functional Network Construction

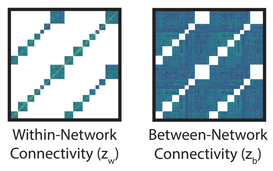


Network Stability Metric

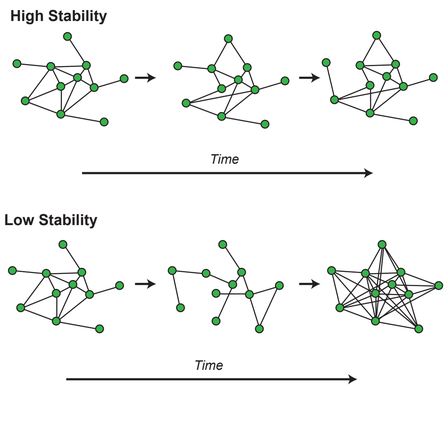


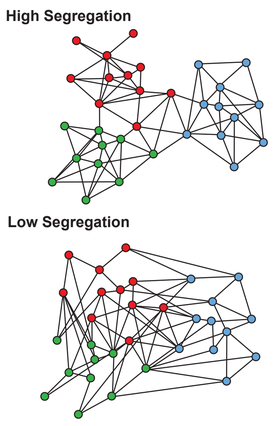
$$Stability = \frac{\sum_{i,j}^{n} r_{ij}}{n}$$

Network Segregation Metric

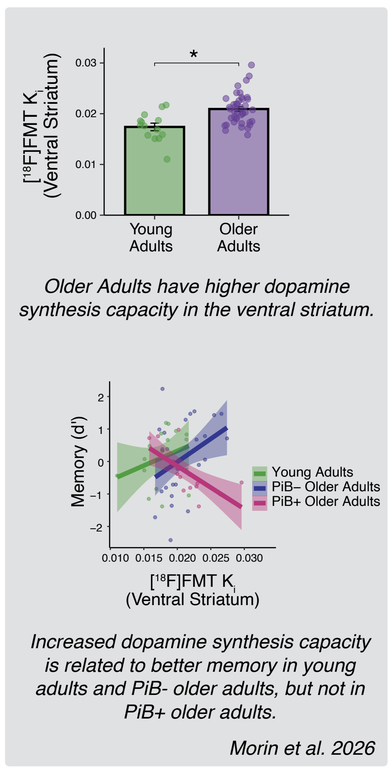


$$Segregation = \frac{\bar{z}_w - \bar{z}_b}{\bar{z}_w}$$

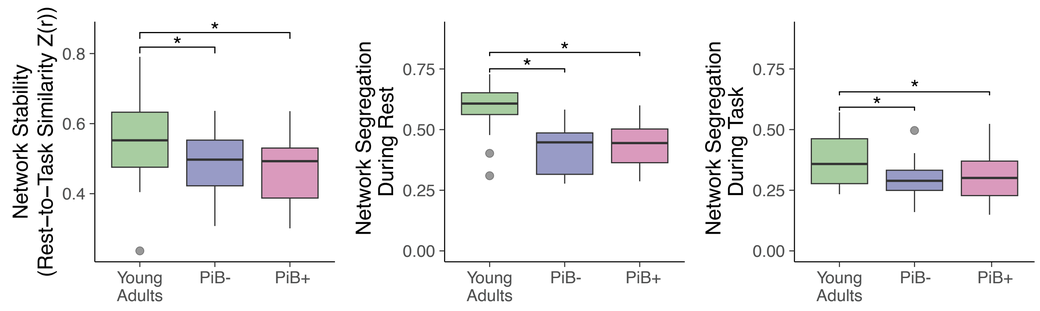




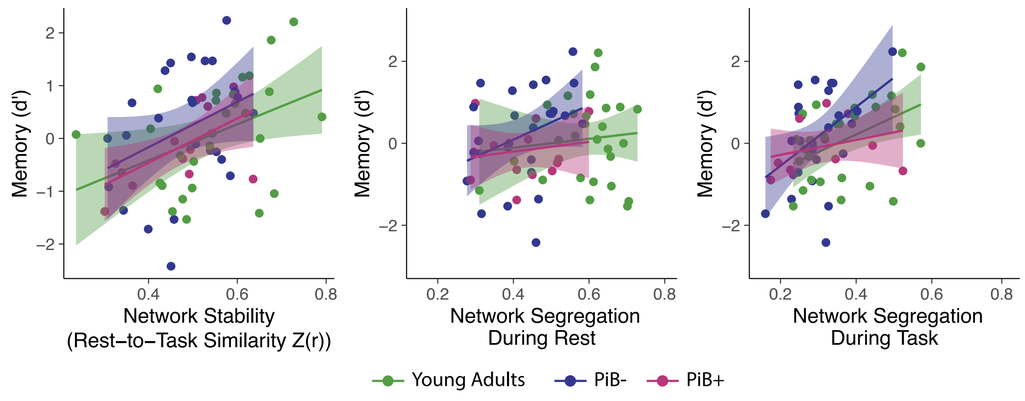
Results



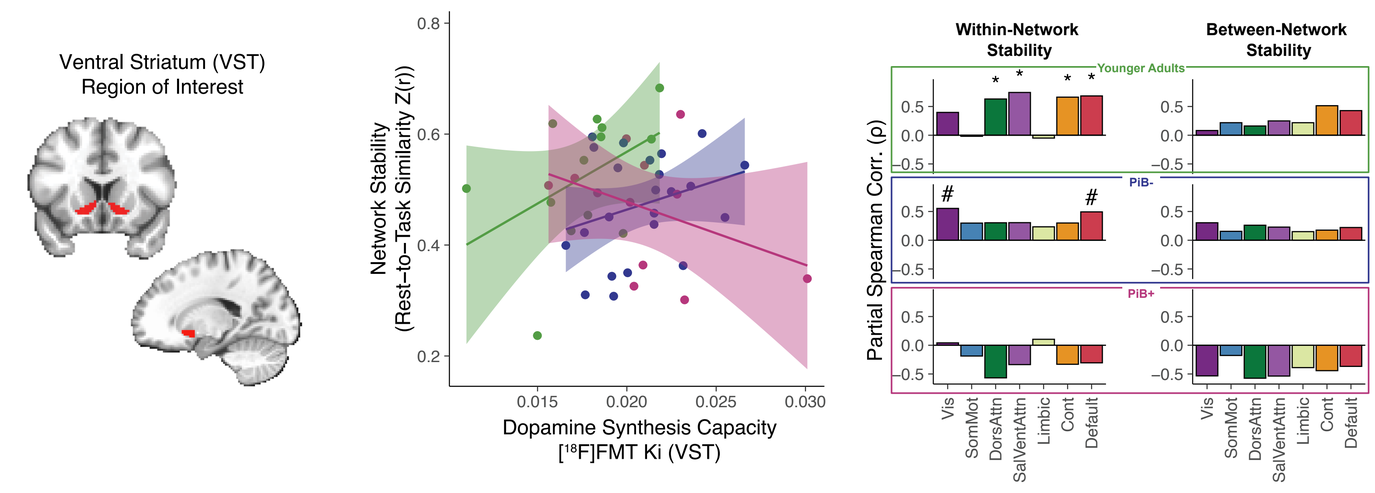
Network Stability and Segregation are Reduced in Older Adults



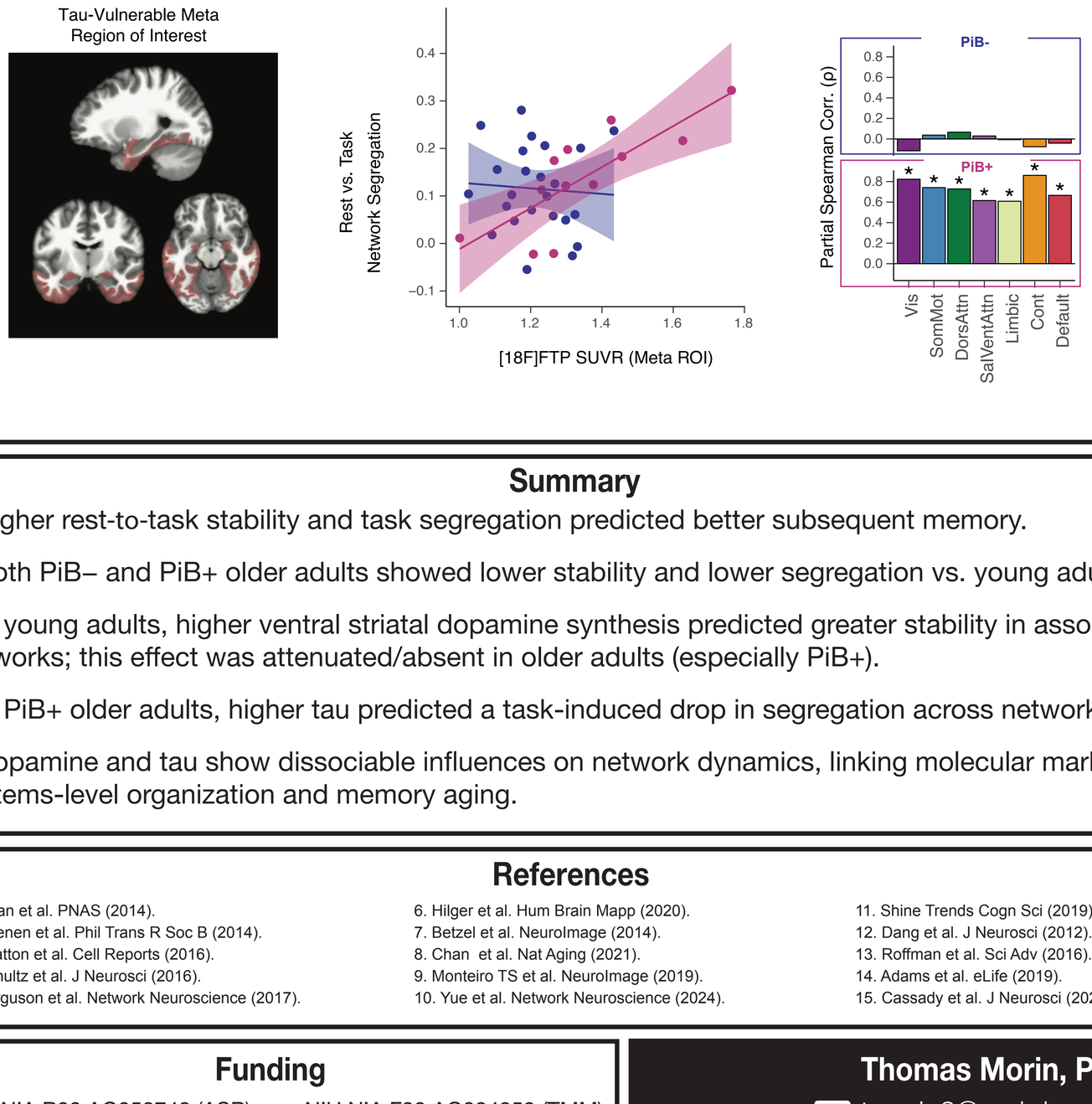
Memory Performance is Associated with Higher Network Stability and Segregation



Dopamine Synthesis Capacity is Associated with Higher Stability in Associative Networks in Young Adults



Tau Burden is Associated with a Task-Induced Drop in Network Integration in PiB+ Older Adults



Summary

- Higher rest-to-task stability and task segregation predicted better subsequent memory.
- Both PiB– and PiB+ older adults showed lower stability and lower segregation vs. young adults.
- In young adults, higher ventral striatal dopamine synthesis predicted greater stability in association networks; this effect was attenuated/absent in older adults (especially PiB+).
- In PiB+ older adults, higher tau predicted a task-induced drop in segregation across networks.
- Dopamine and tau show dissociable influences on network dynamics, linking molecular markers to systems-level organization and memory aging.

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