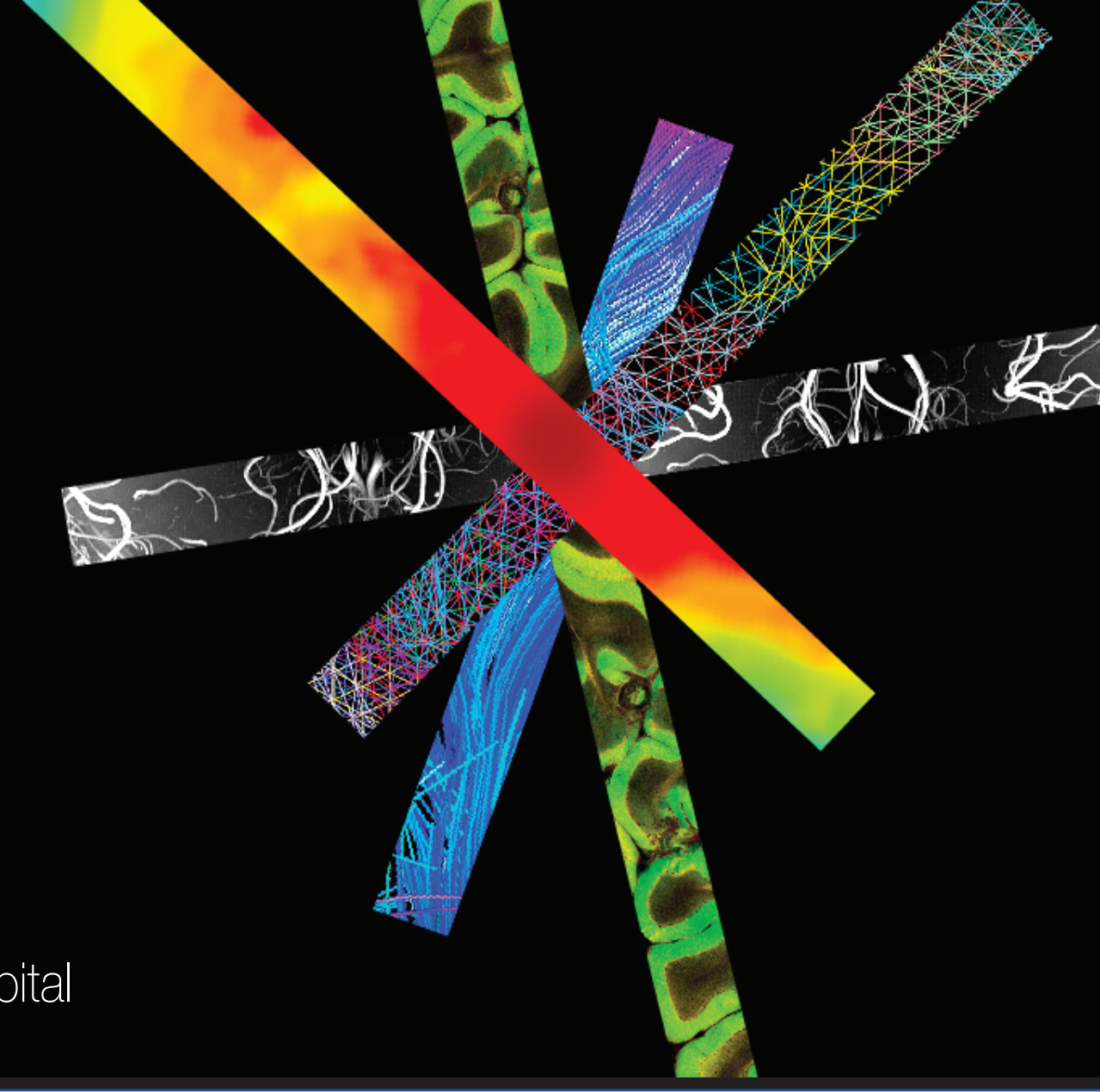


D2/3 receptor occupancy measured with $[^{11}\text{C}]$ -raclopride and functional brain network reconfiguration in healthy older adults

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Background

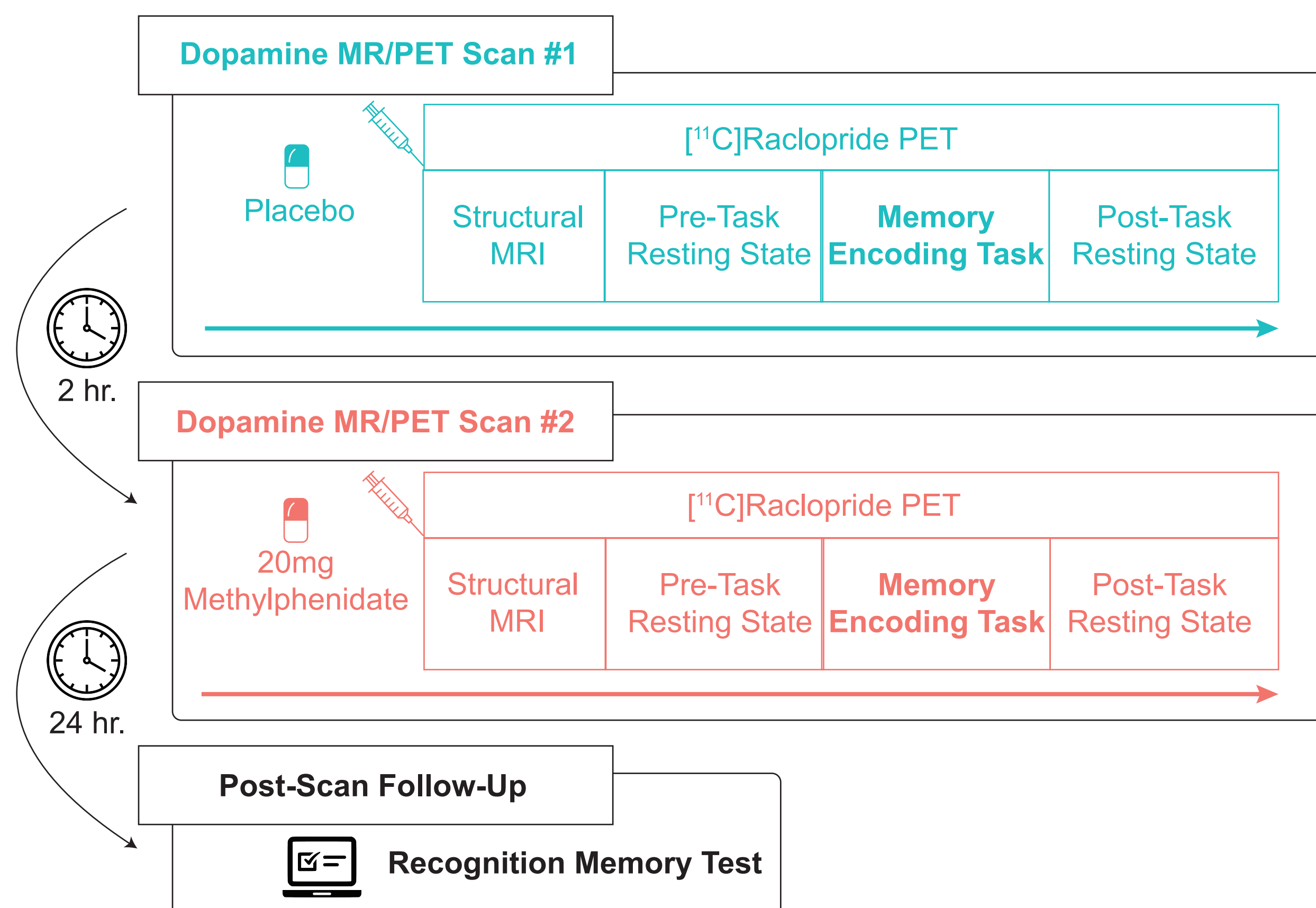
- Aging is associated with declines in both the dopamine system and in memory ability.^{1,2}
- Methylphenidate increases the availability of dopamine at the synapse by inhibiting reuptake.^{3,4}
- Dopamine availability may be related to functional network stability/flexibility.^{5,6,7,8}
- Functional brain network stability is associated with better cognitive performance on a variety of tasks.^{9,10,11}

Research Questions:

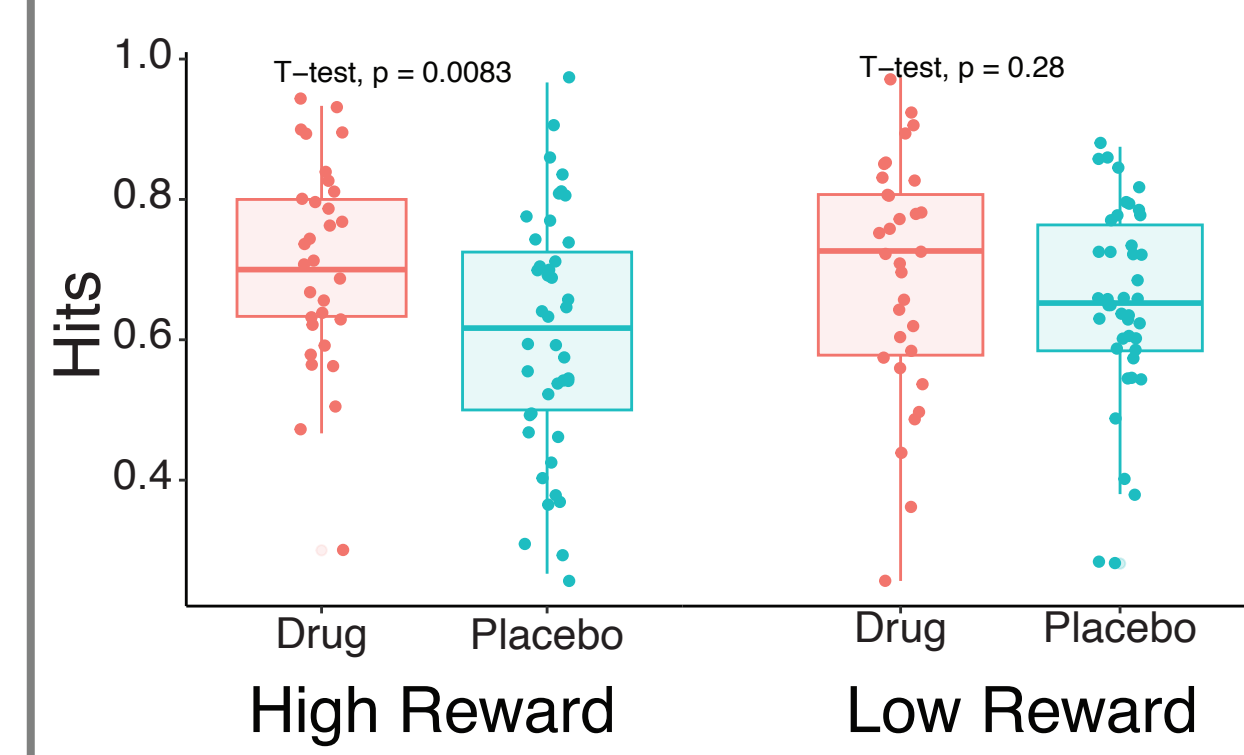
- Does methylphenidate facilitate improved memory for rewarding stimuli?
- Is D2/3 receptor binding potential related to functional network reconfiguration in older adults?
- Is reward-memory associated with dopamine-related functional network reconfiguration?

Study Procedure

Participants: Healthy older adults (Age 60 - 80; n = 45)

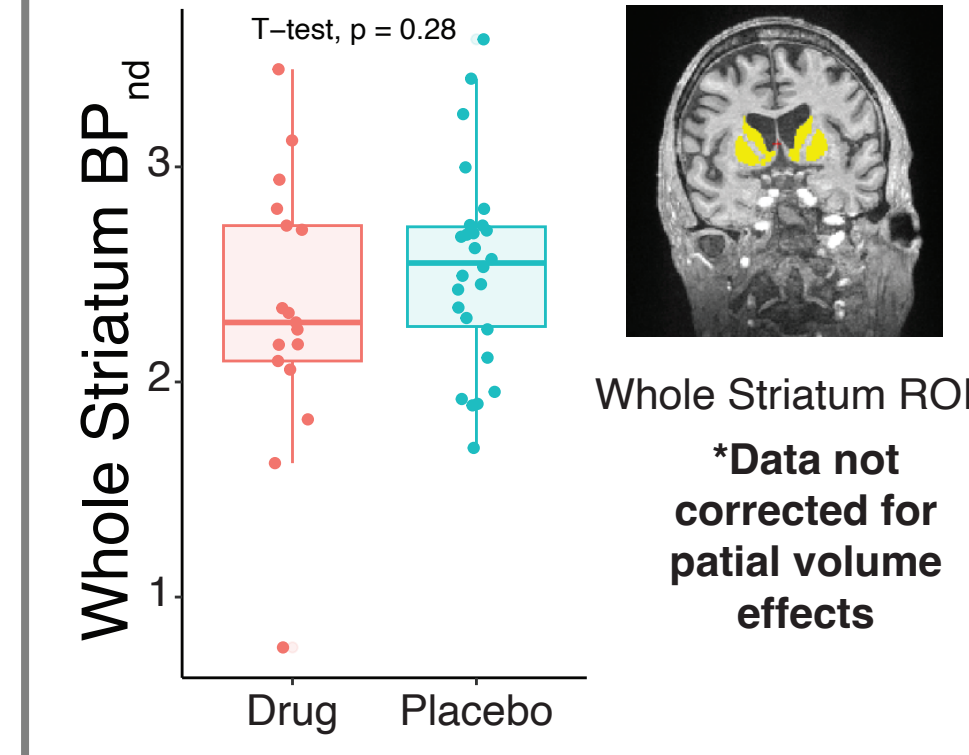


Memory Results



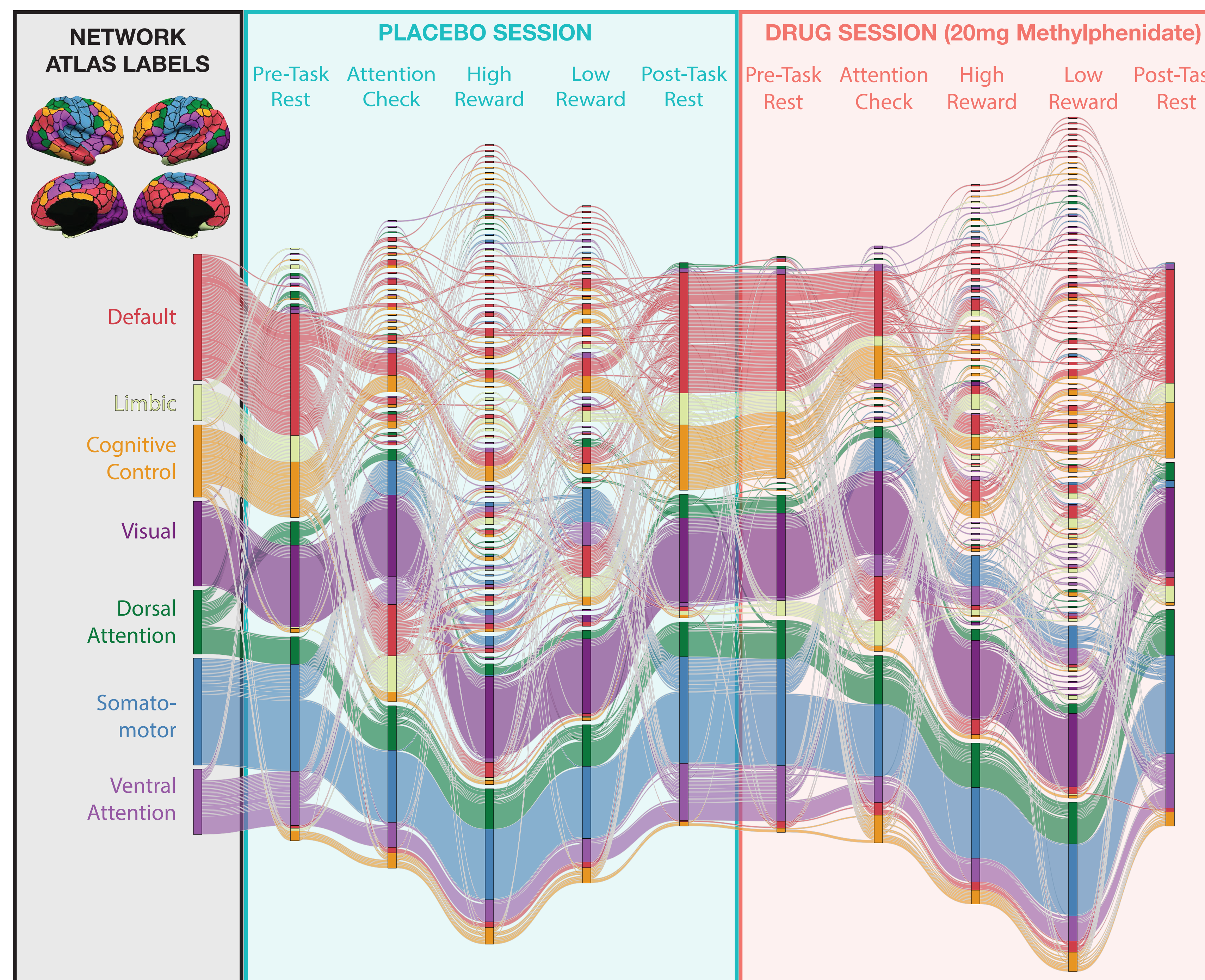
• Overall participants had better memory for stimuli viewed during the **Drug Session**.
($F = 6.29, p < 0.05$)

$[^{11}\text{C}]$ Raclopride Binding Potential

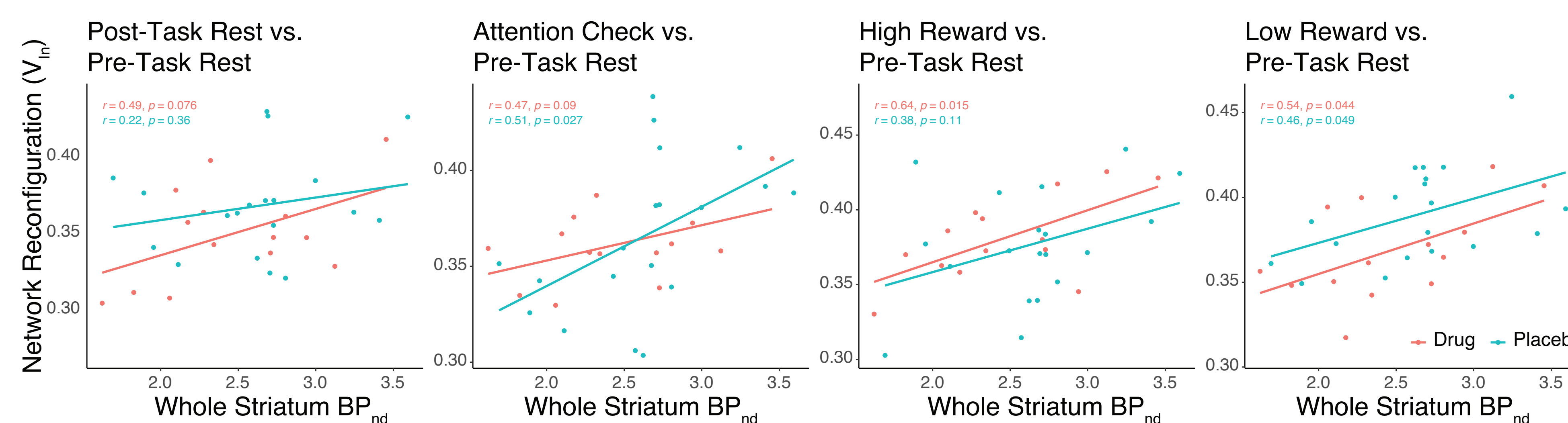


• Preliminary PET data does not detect a significant change in whole-striatum BP_{nd} between placebo and drug scans.

Functional Network Reconfiguration Across Rest and Task Conditions

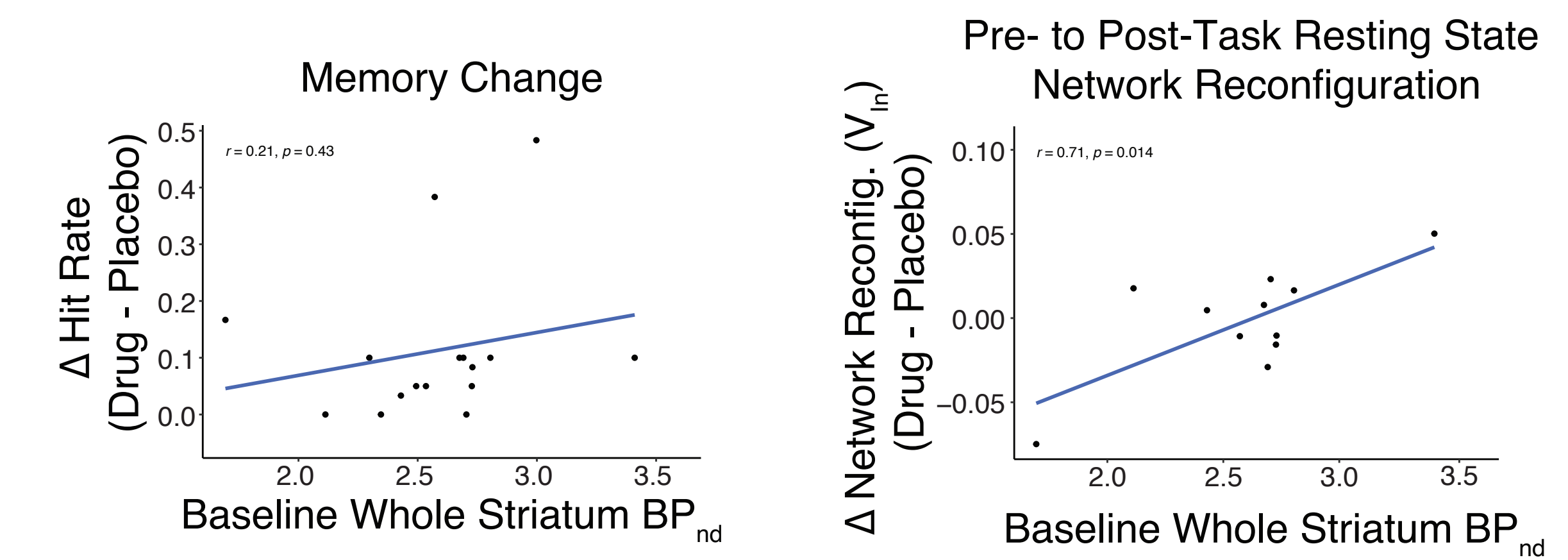


Network Reconfiguration and Whole Striatum Binding Potential



• Greater whole striatum BP_{nd} is associated with increased functional network reconfiguration.

Preliminary Analysis: Does Baseline Binding Potential Affect Drug-Induced Changes in Memory and Network Reconfiguration?



• Higher baseline BP_{nd} *might* be associated with better drug-induced memory improvement.

• Higher baseline BP_{nd} appears to be associated with larger drug-induced increases in pre-to-post task resting state network reconfiguration.

Summary & Conclusions

- Methylphenidate enhances memory (especially for high-reward stimuli).
- Increased striatal binding potential is associated with greater functional network reconfiguration.
- Prior work by Cools & D'Esposito (2011) suggests that baseline striatal binding potential may affect the degree of drug-induced changes in memory scores. Our preliminary analysis supports this framework.

This preliminary evidence suggests a link between dopamine availability, functional network reconfiguration, and reward-memory in older adults.

References

1. Backman et al. 2010. *Neuro. & Biobeh. Rev.*
2. Backman et al. 2006. *Neuro. & Biobeh. Rev.*
3. Berry et al. 2018. *Neuropsychopharmacology.*
4. Kuczenski & Segal. 1997. *J. Neurochemistry.*
5. Braun et al. 2016. *PNAS.*
6. Braun et al. 2021. *Nature Communications.*
7. Garret et al. 2022. *Preprint.*
8. Roffman et al. 2017. *Scientific Advances.*
9. Morin et al. 2023. *Cerebral Cortex.*
10. Hilger et al. 2020. *Human Brain Mapping.*
11. Hearne et al. 2017. *J. Neuroscience.*
12. Schaefer et al. 2018.
13. Cools & D'Esposito. 2011. *Biol. Psychiatry.*

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