Network Specificity and Age Differences in Predicting Executive Functioning from Brain Connectivity

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Introduction

- **Healthy aging** is associated with altered **executive functioning** (EF)
- Age-related differences in EF abilities are related to changes in **resting-state functional connectivity** (RSFC) **within brain networks** associated with EF [1]
- However, it remains unclear which role RSFC within EF-associated networks plays as a marker for individual EF performance
- Here, we examined to what degree individual EF abilities can be predicted from RSFC in i) an EF-associated network, ii) a perceptuomotor network, iii) the whole-brain connectome, and iv) random networks in young and old adults

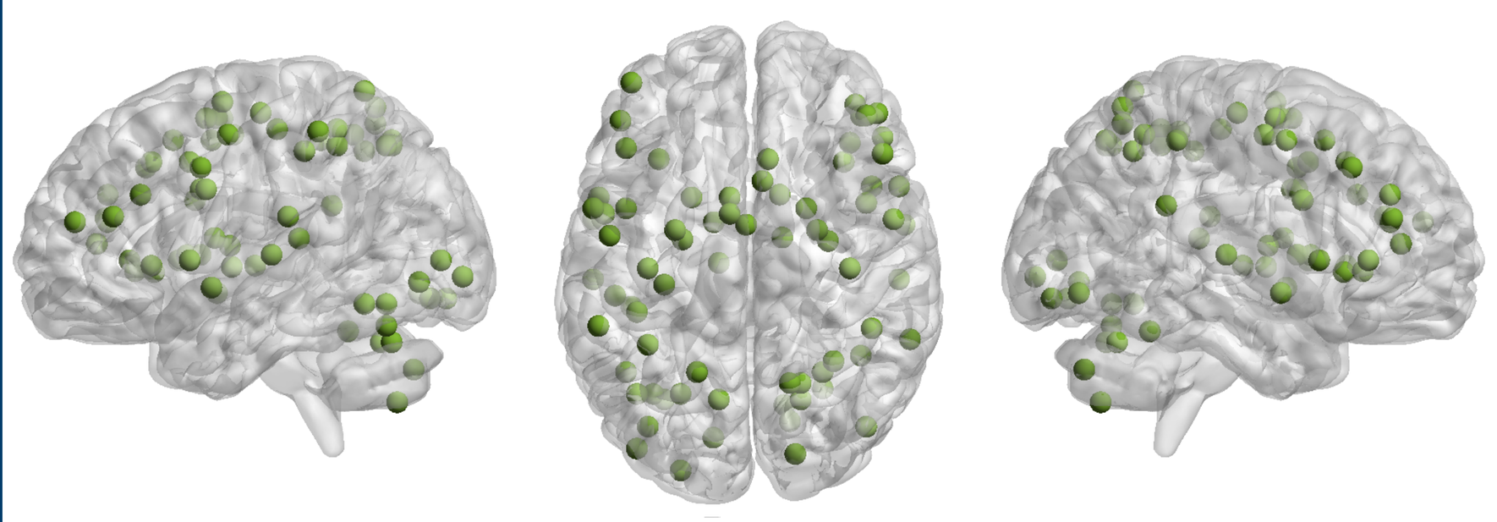
Research Questions:
a) Do young and old adults differ in the predictability of their EF abilities depending on network or task demand level?
b) Does an EF-related network outperform EF-unrelated networks?
c) Does this pattern change with demand level?

Methods

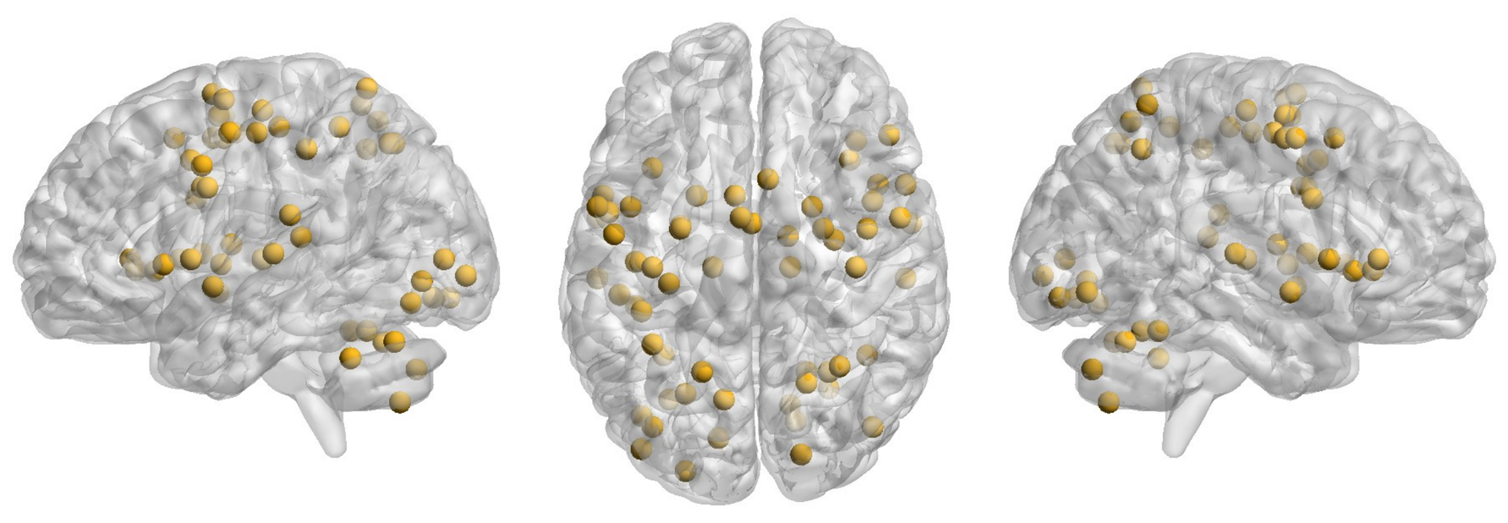
- We meta-analytically defined an **EF-related network** (EFN) [2] and a **perceptuomotor network** (PercMot) [3] linked to visual, auditory, and motor processing
- As a **whole-brain control** we used Power et al.'s [4] graph of functional areas
- Further, we created 10 **random networks** (RandomAvg) of 50 nodes preserving the spatial properties of the EFN [5]
- Resting-state fMRI and behavioral data of **116 younger** (age = 20-40 years, 64 females) and **111 older** (age = 60-80 years, 72 females) healthy adults were obtained from the **enhanced NKI sample** [6]
- Target variables comprised performance in cognitively **highly demanding** (HD) and **less demanding** (LD) conditions of each of **3 classic EF tasks**: Color–Word Interference, Trail Making, and N-Back
- Individual z-transformed performance scores were then predicted from each network's RSFC using **partial least squares** with 100 repetitions of a 10-fold cross-validation scheme
- Differences in predictions were further investigated using **mixed-measures ANOVA**

Results

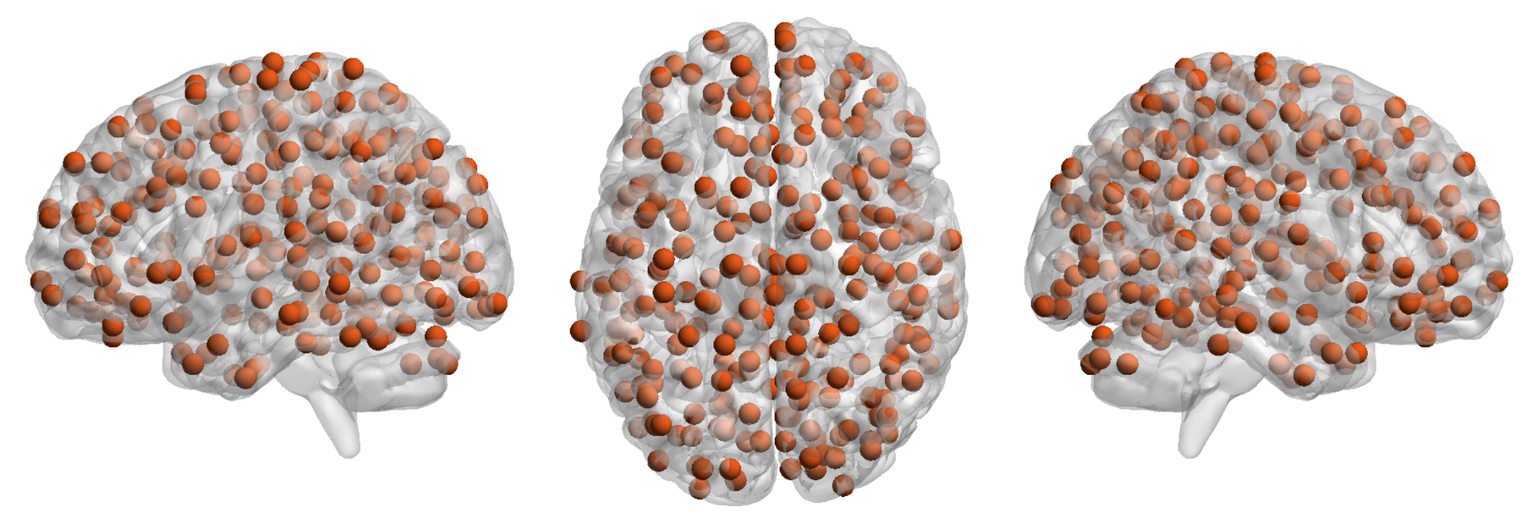
Meta-analytically defined EF-related network



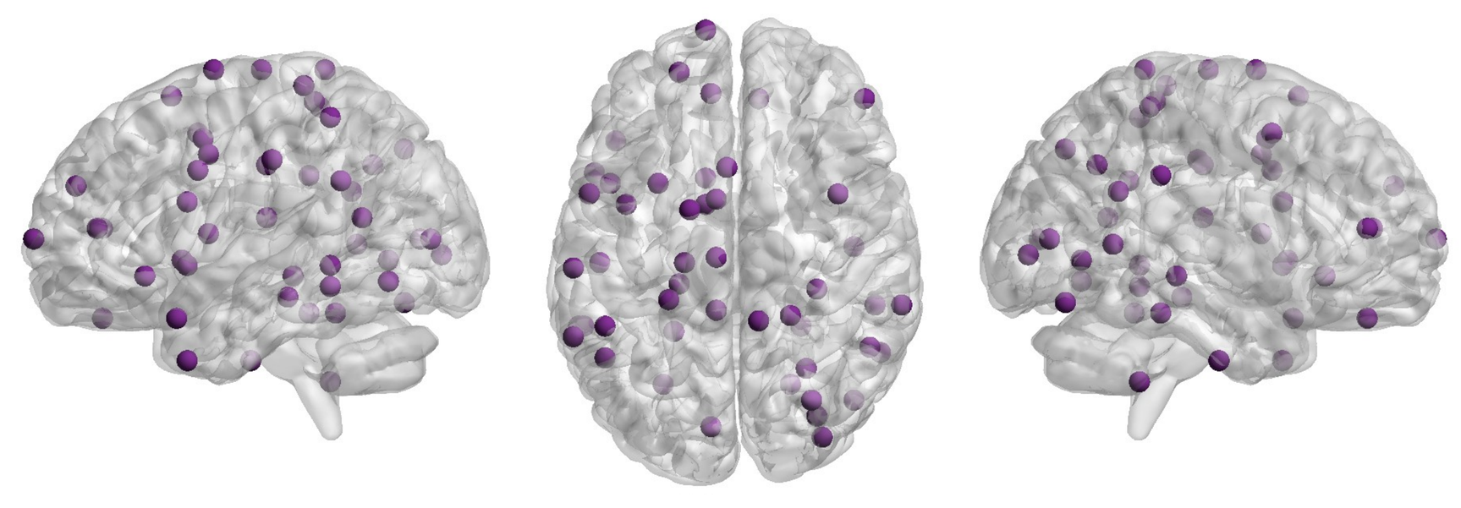
Meta-analytically defined perceptuomotor-related network



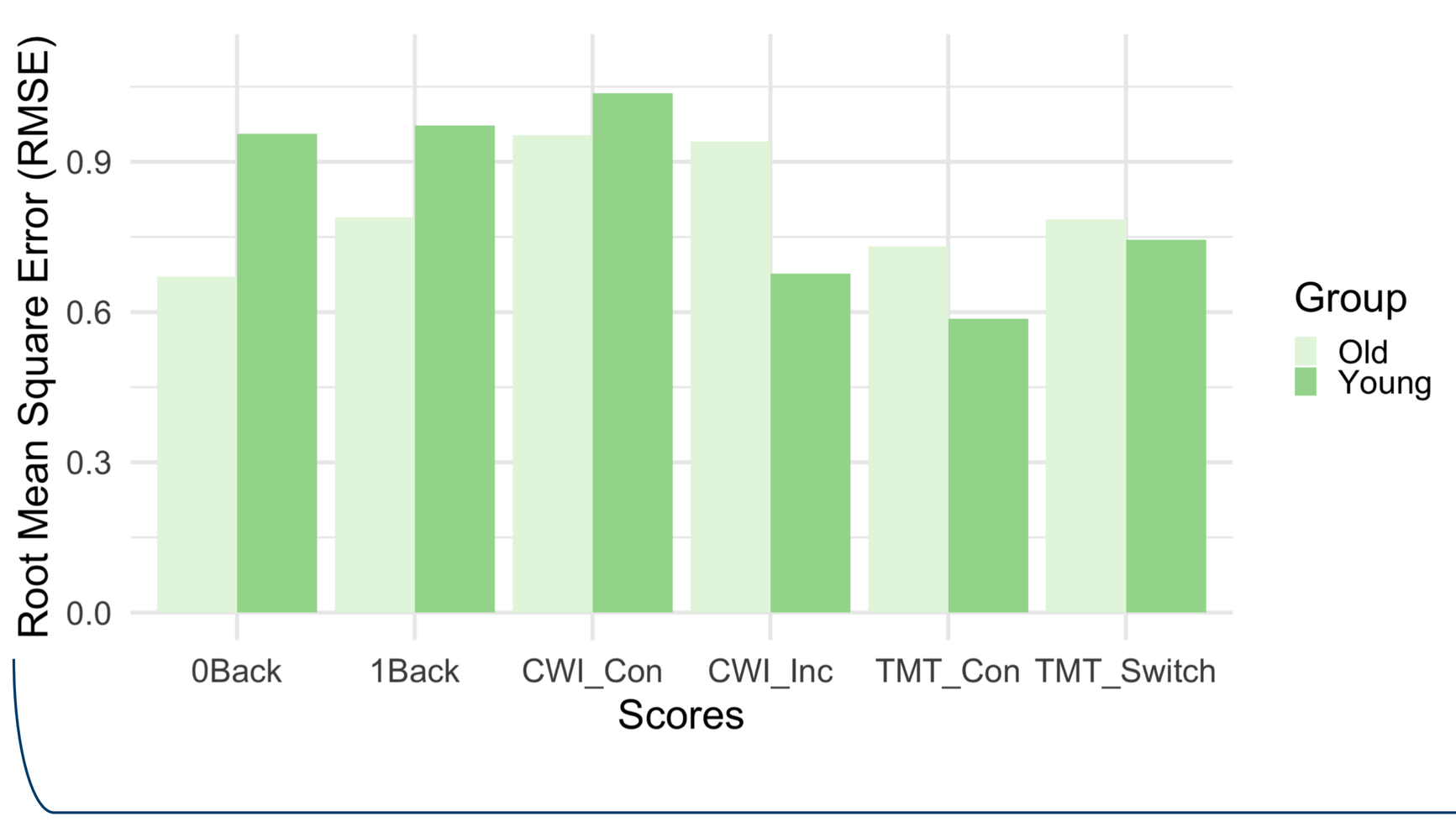
Whole brain represented by Power et al.'s (2011) graph of cortical functional areas

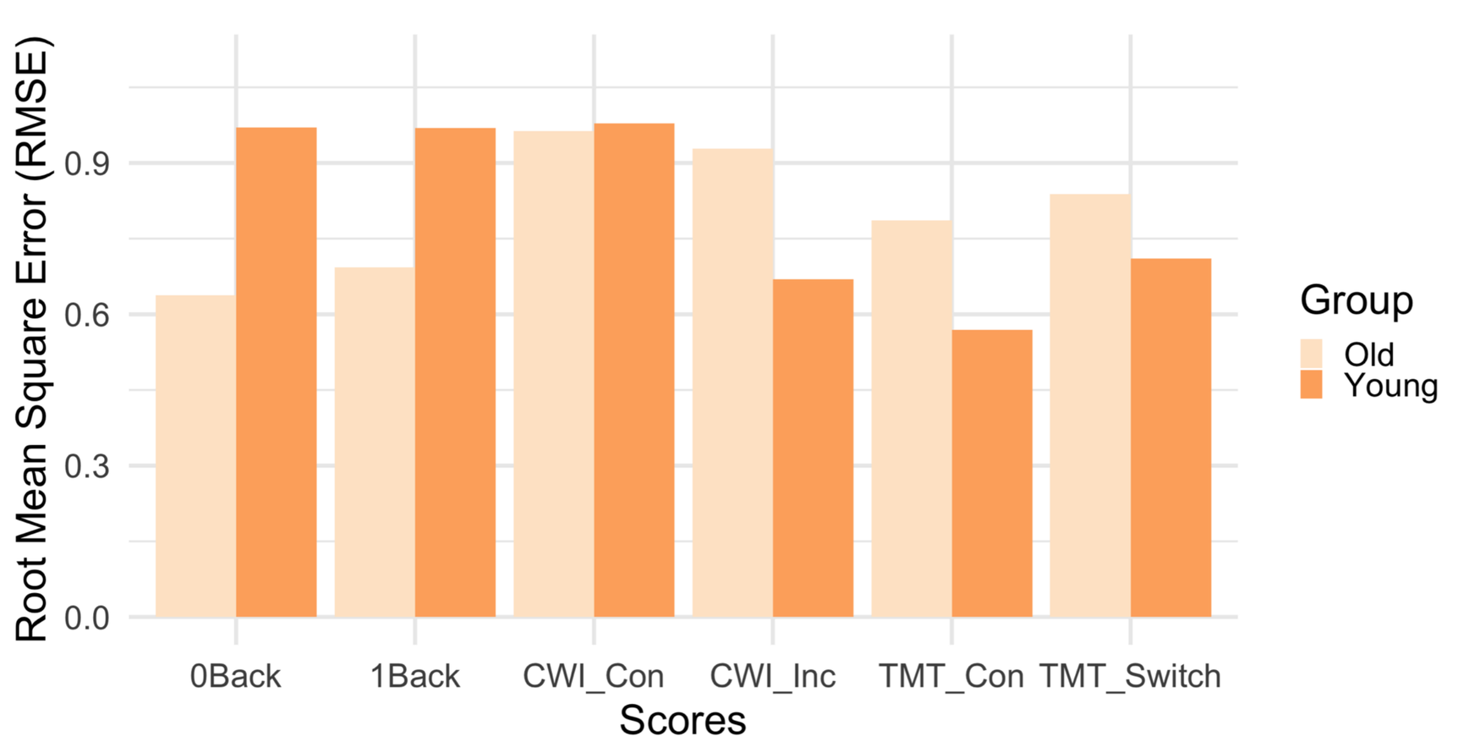


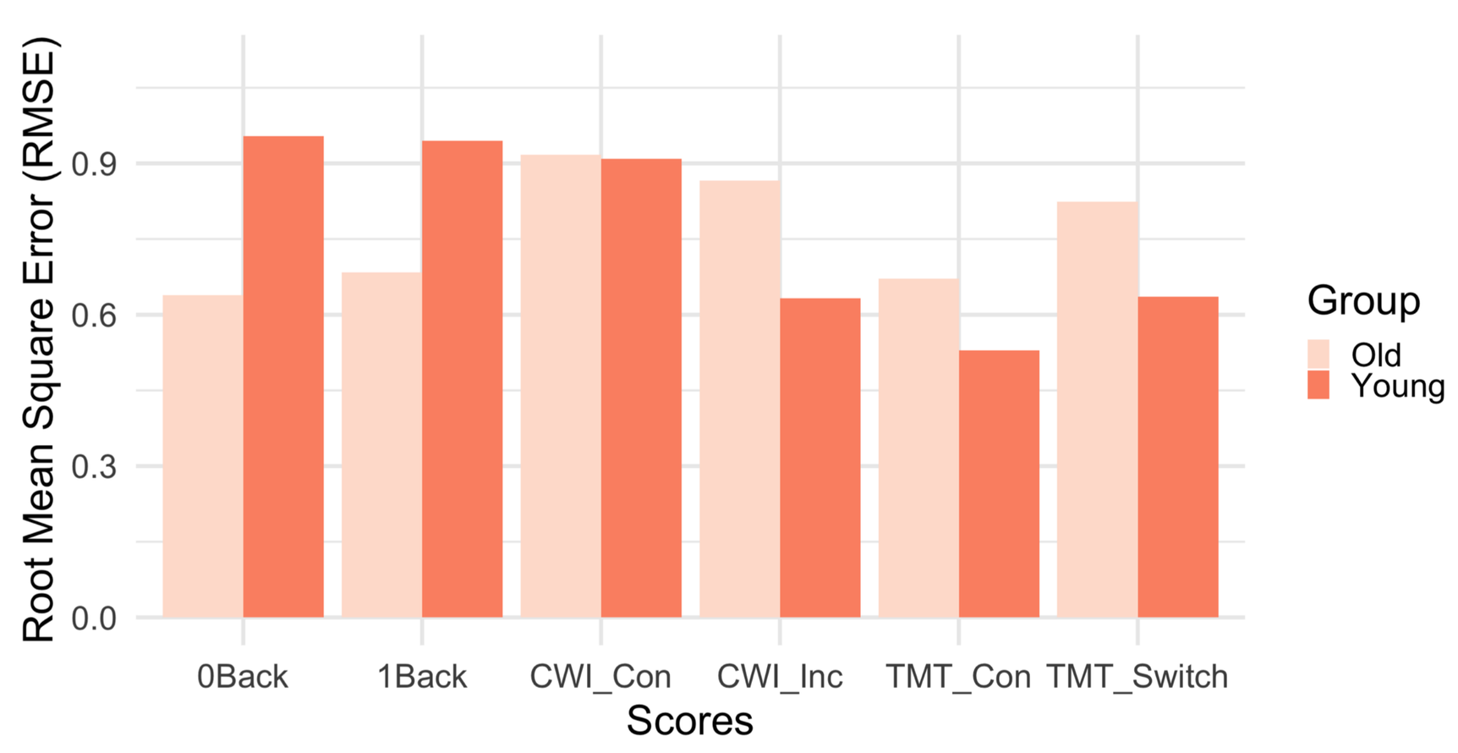
Example random network

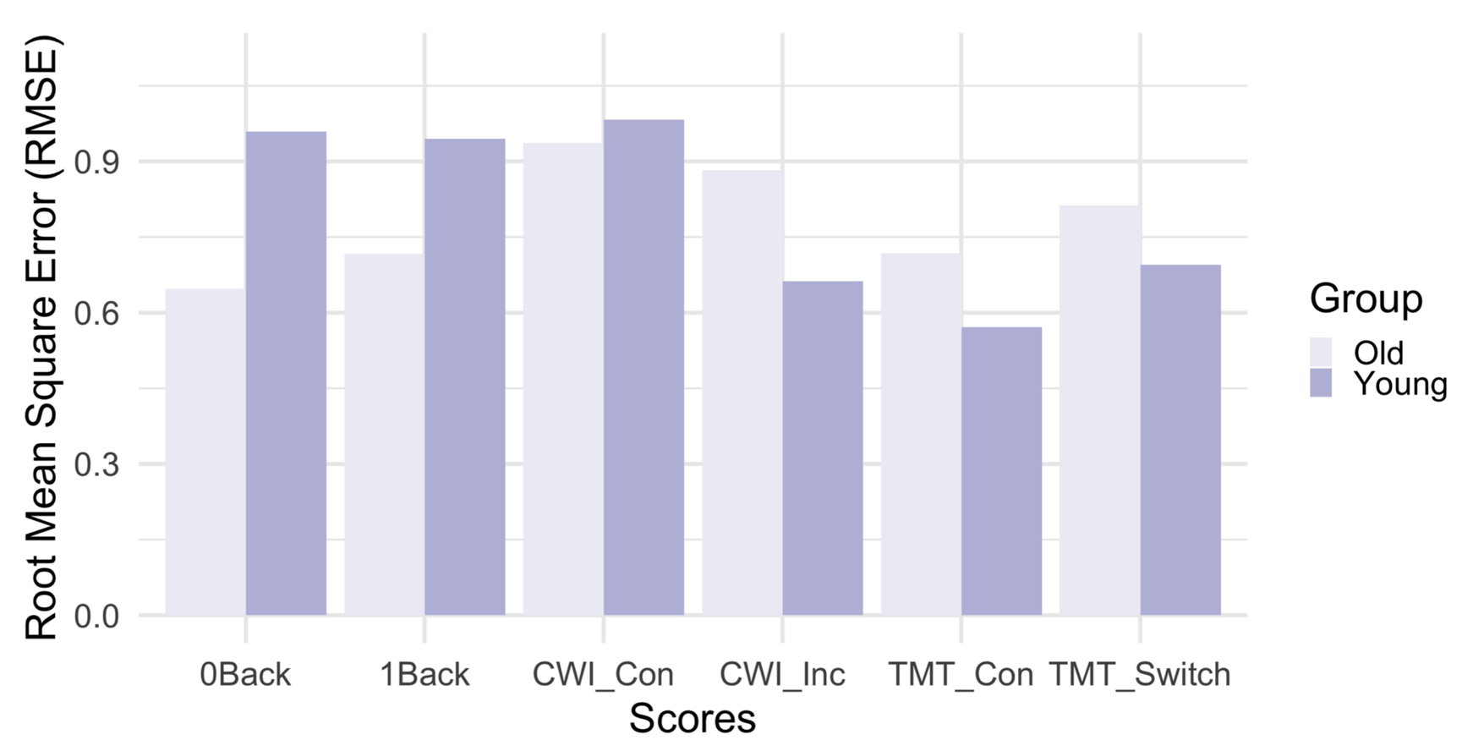


Prediction



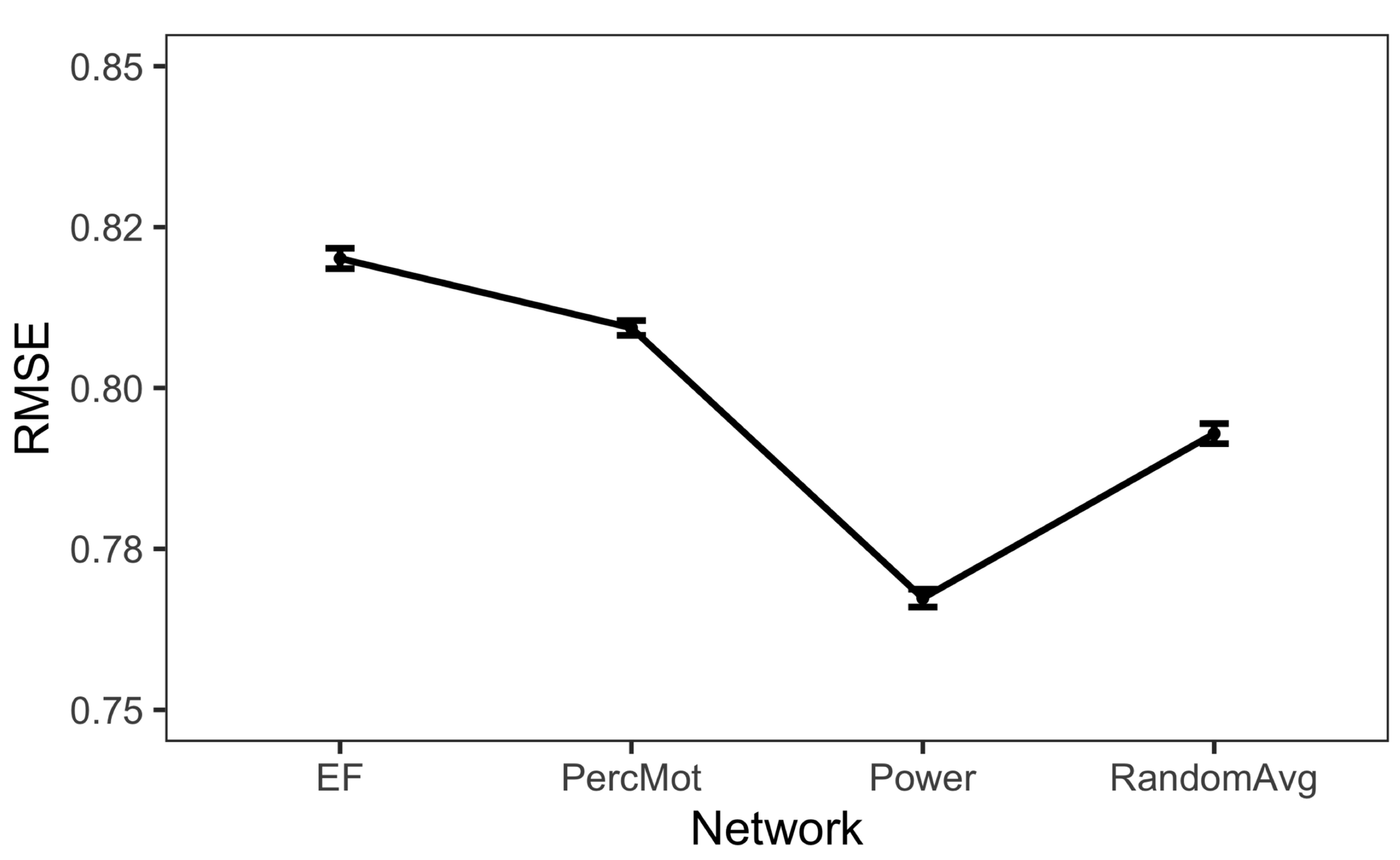




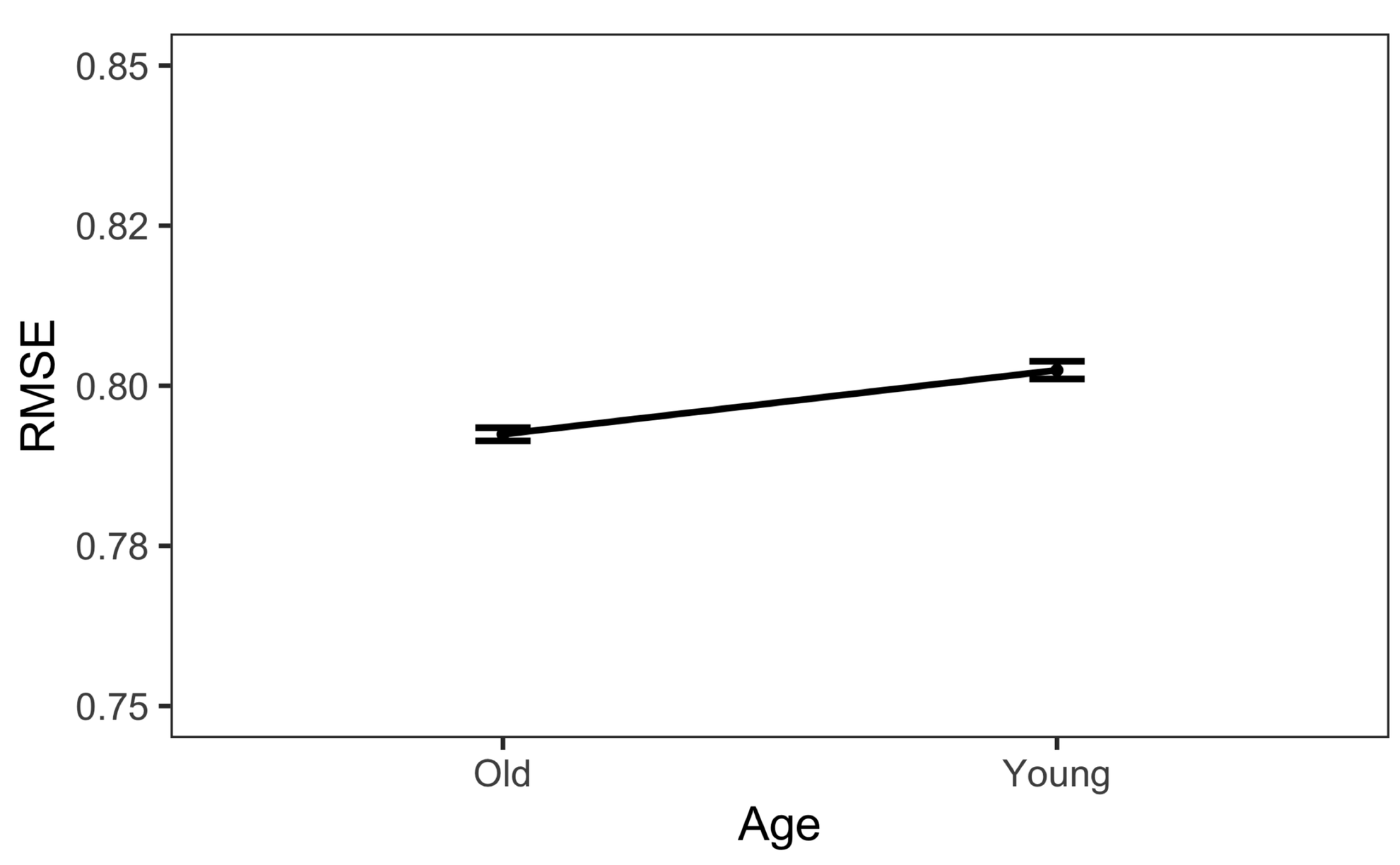


ANOVA Main Effects

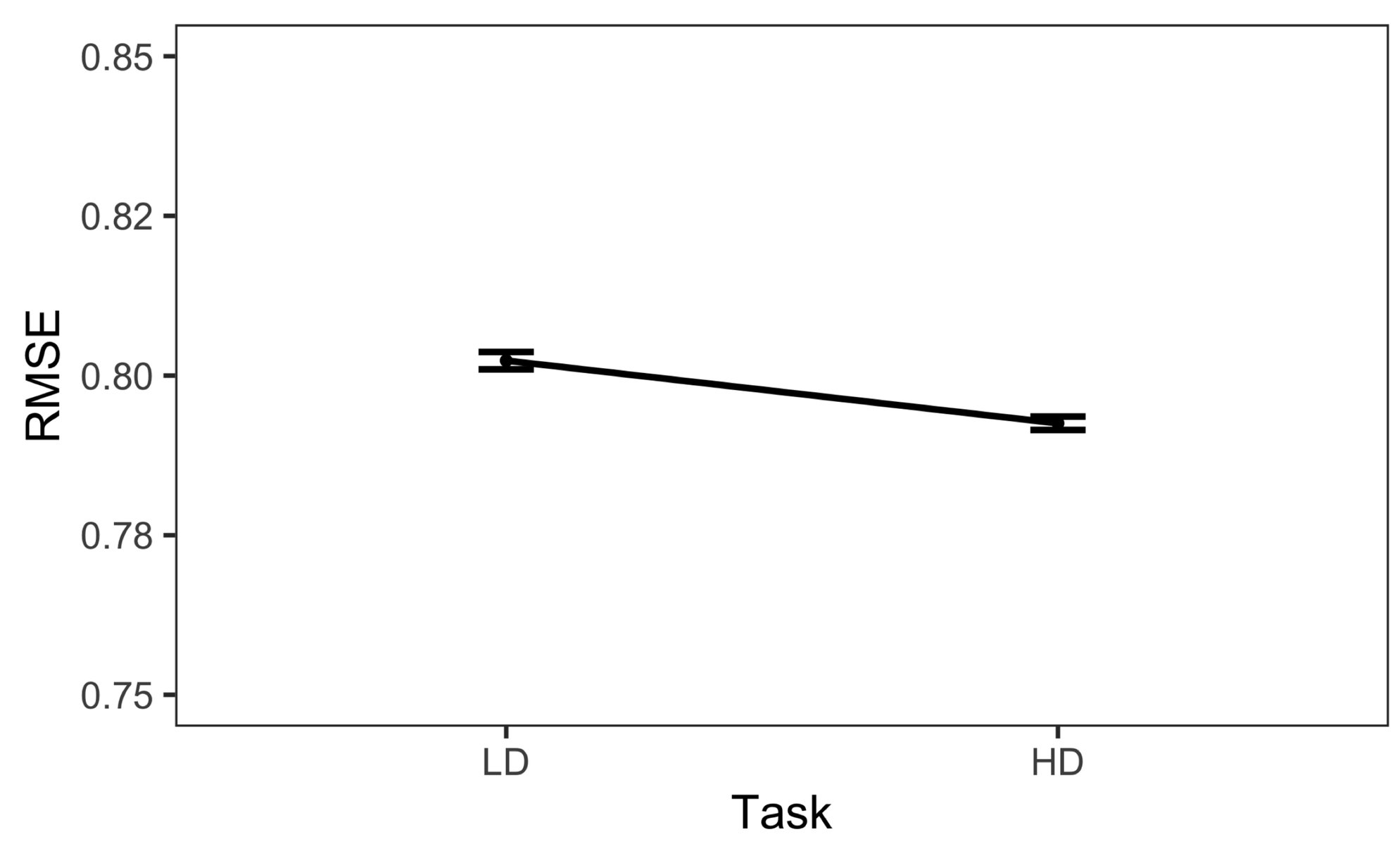
Network



Age

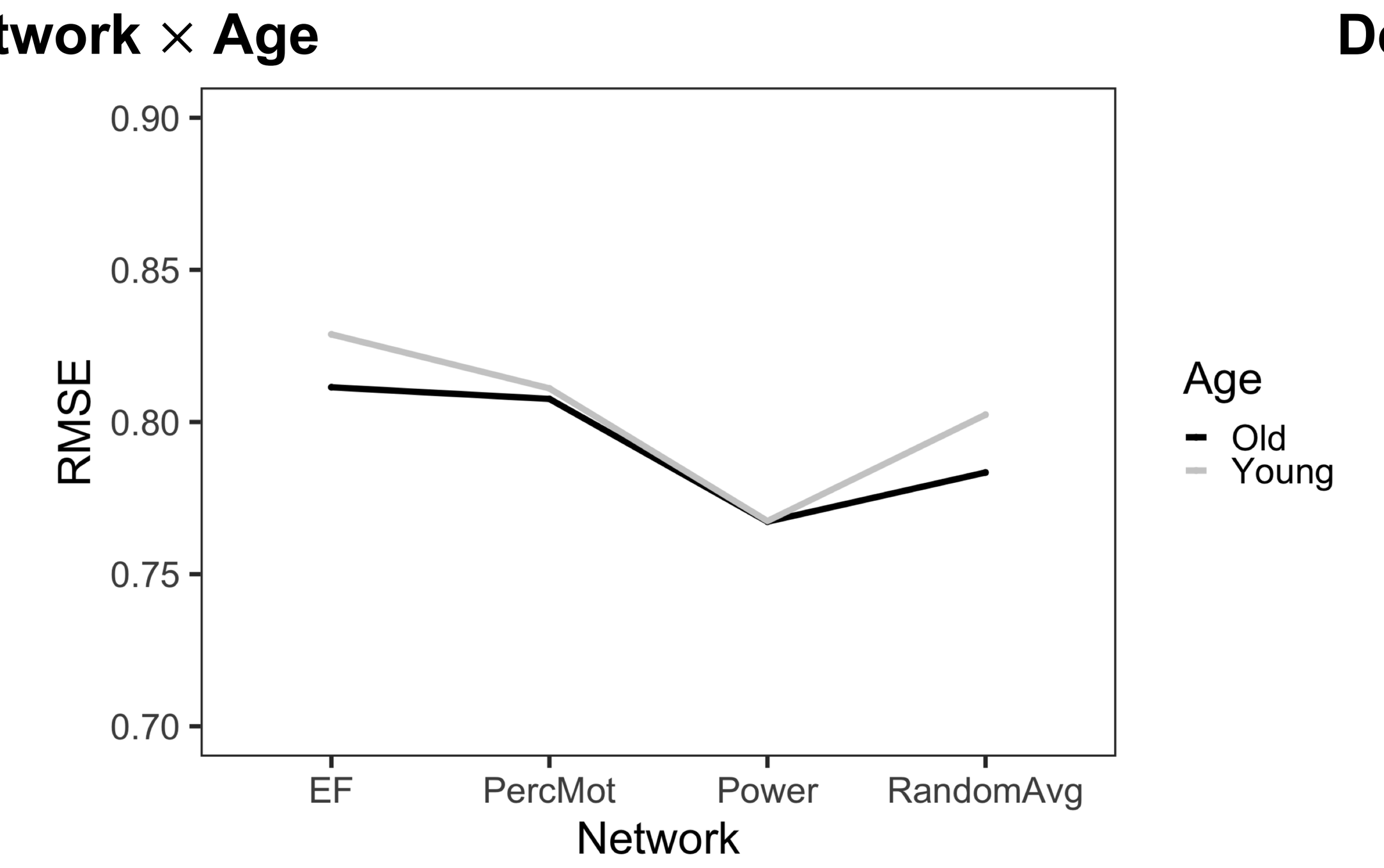


Demand Level

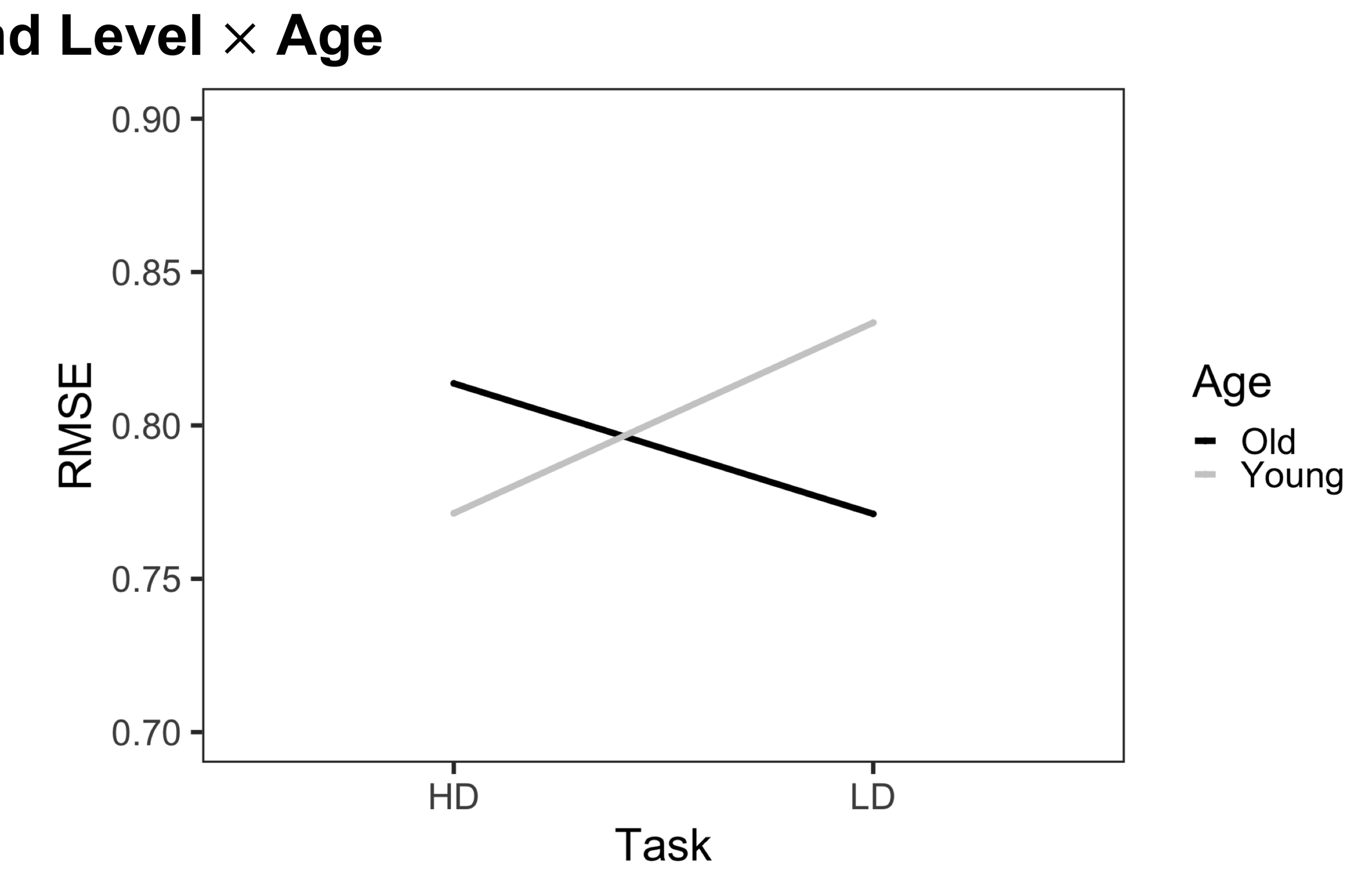


ANOVA Interaction Effects

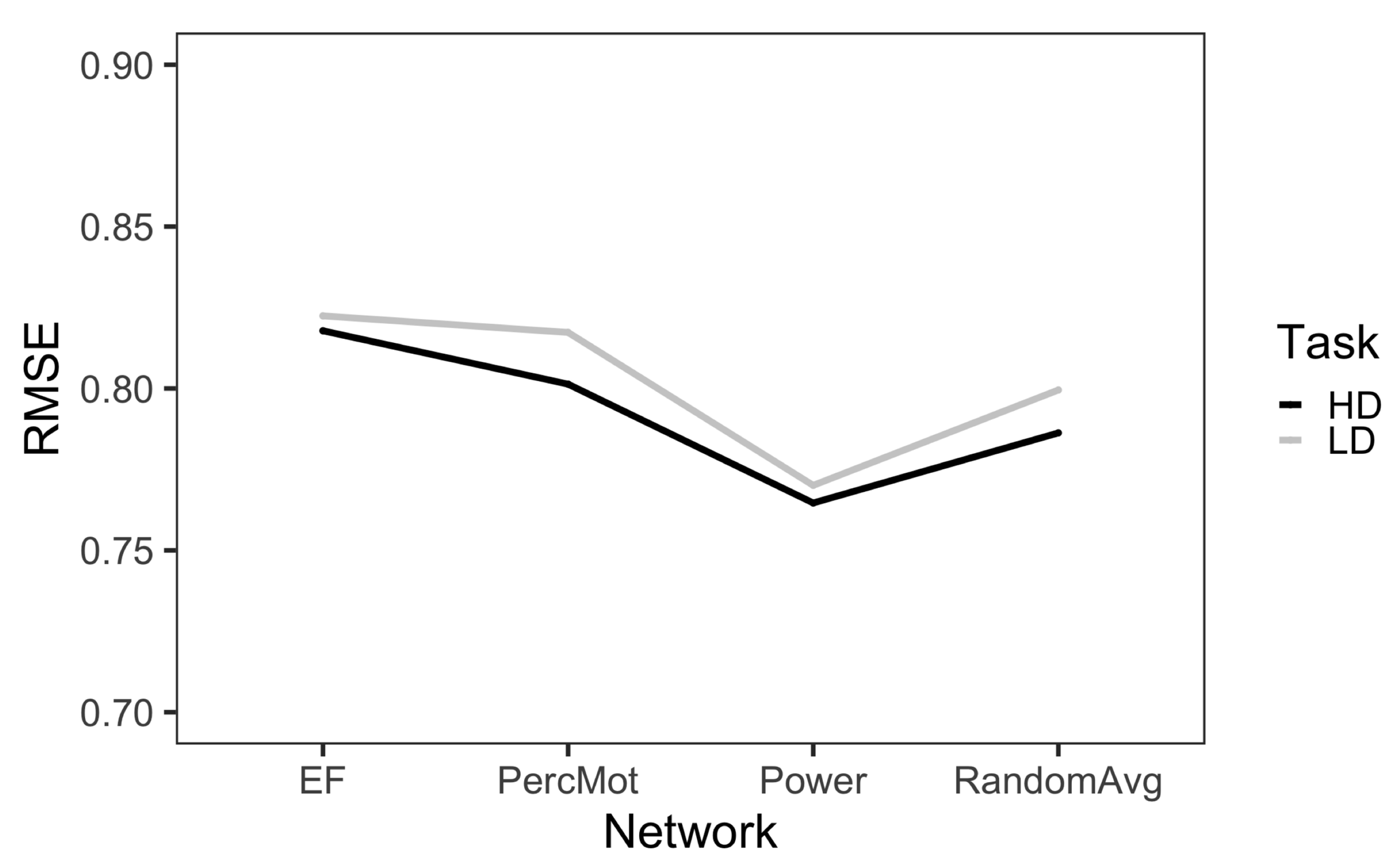
Network × Age



Demand Level × Age



Demand Level × Network



Discussion

- A comprehensive, robustly defined **EFN is not better at predicting EF abilities** than are EF-unrelated networks
- Brain regions crucial but not specific to EF – e.g., **modulating between-network communication** – might be missing from the meta-analytically derived network
- **Brain–behavior associations increase with advancing age** [7]
  - i) greater behavioral variance in older adults?
  - ii) global properties like **overall-atrophy**?
  - iii) **less brain variability** in older adults? **Younger brains might exploit possible functional architectures more efficiently** [8]
- Task × age interaction: **age-related decline in within-network specificity or segregation between networks** [9]
- Within-network connectivity might be more important in LD tasks – between-network connectivity more so in HD tasks [10]

Conclusions:
- ***Lack of specificity of neurobiologically plausible networks for predicting EF abilities***
- ***Global properties of the brain or between-network communication might contain more information about inter-individual differences in EF abilities***
- ***Replication with different modalities (e.g., grey matter volume) and states (e.g., task) necessary***

References: [1] Langner, R. (2015), 'Aging and response conflict solution: behavioural and functional connectivity changes'; Steffener, J., et al. (2009), 'The Impact of Age-Related Changes on Working Memory Functional Activity'. [2] Worringer, B., et al. (2019), 'Common and distinct neural correlates of dual-tasking and task-switching: a meta-analytic review and a neuro-cognitive processing model of human multitasking'; Langner, R., et al. (2018), 'Towards a human self-regulation system: Common and distinct neural signatures of emotional and behavioural control'; Rottschy, C., et al. (2012), 'Modelling neural correlates of working memory: A coordinate-based meta-analysis'. [3] Heckner, M.K., et al. (2021), 'Delineating visual, auditory and motor regions in the human brain with functional neuroimaging: A BrainMap-based metaanalytic synthesis'. [4] Power, J.D., et al. (2011). 'Functional network organization of the human brain'. [5] https://github.com/MartinGell/random_nets [6] Nooner, K., et al. (2012), 'The NKI-Rockland Sample: A model for accelerating the pace of discovery science in psychiatry'. [7] Pläschke, R., et al. (2020), 'Age differences in predicting working memory performance from network-based functional connectivity'; Lockhart, S.N., et al. (2014), 'Structural Imaging Measures of Brain Aging'. [8] McIntosh, A., et al. (2010), 'The development of a noisy brain'; Garrett, D.D., et al. (2011), 'The importance of being variable'. [9] Chan, M.Y., et al., (2017), 'Resting-State Network Topology Differentiates Task Signals across the Adult Life Span'; Varangis, E., et al., (2019), 'The Affect of Aging on Resting State Connectivity of Predefined Networks in the Brain'. [10] Cohen, J.R., & D'Esposito, M. (2016), 'The Segregation and Integration of Distinct Brain Networks and their Relationship to Cognition'; Yue, Q., et al., (2017), 'Brain Modularity Mediates the Relation between Task Complexity and Performance'.

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