

Marisa K. Heckner^{1,2,*}, Edna C. Cieslik^{1,2}, Kaustubh R. Patil^{1,2}, Simon B. Eickhoff^{1,2}, Felix Hoffstaedter^{1,2}, & Robert Langner^{1,2}

¹Institute of Systems Neuroscience, Heinrich Heine University Düsseldorf, Düsseldorf, Germany; ²Institute of Neuroscience and Medicine (INM-7: Brain and Behaviour), Research Centre Jülich, Jülich, Germany, *contact: m.heckner@fz-juelich.de

Introduction

- **Healthy aging** is associated with altered behavioral performance and brain activation patterns in **executive functions (EFs)**
- The neural correlates of these changes, however, remain unclear
- Earlier studies reported age-related differences in **resting-state functional connectivity (RSFC)**, **grey-matter volume (GMV)** and **regional homogeneity (ReHo)** within brain networks associated with EFs [1,2,3]
- The current study aimed to gain a better understanding of the neural implementations of EFs and its change throughout the lifespan

We therefore

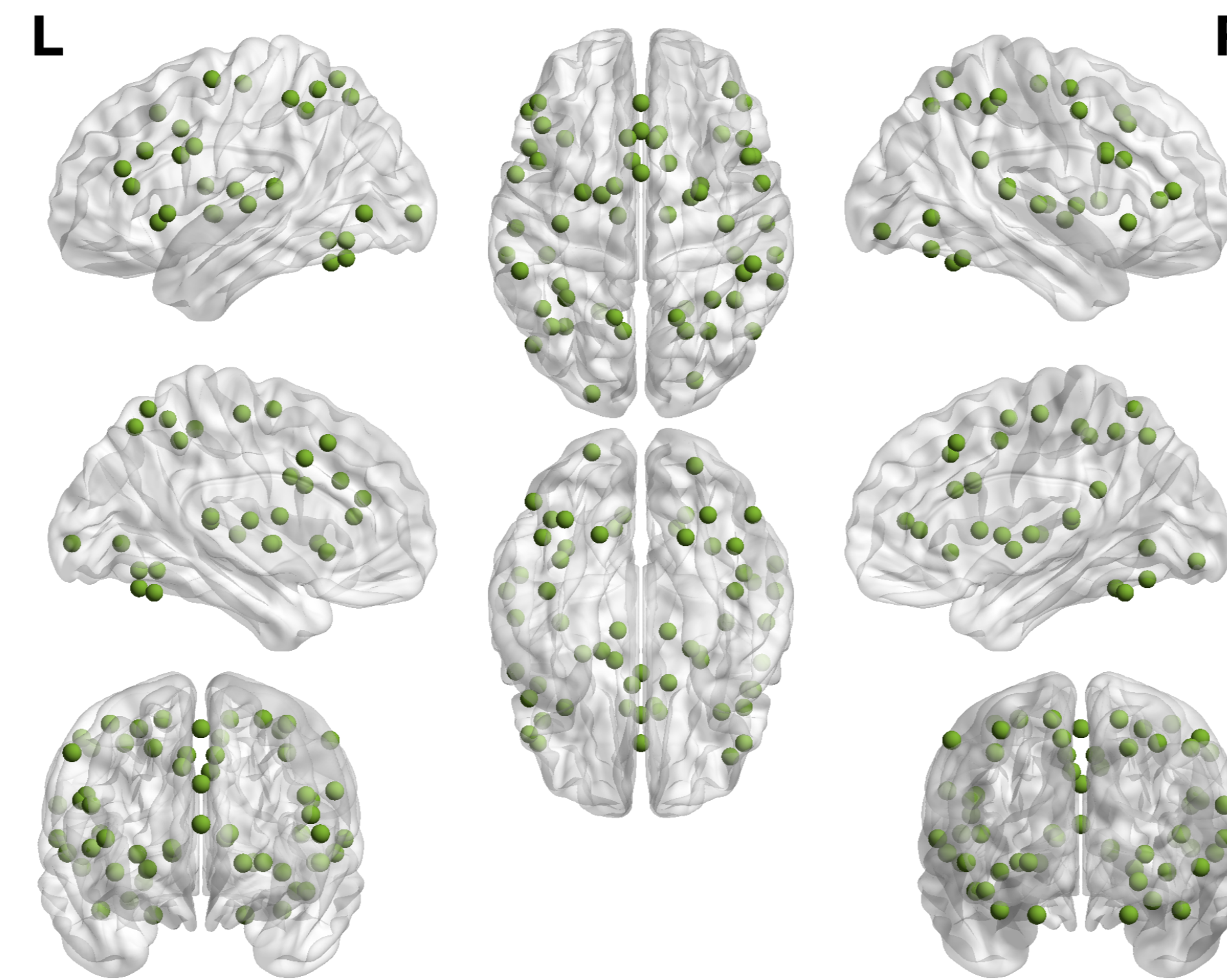
- defined an extended EF-network (eEFN) based on meta-analyses, reflecting diverse EF-facets and then**
- examined to what degree individual abilities in three important EF-subcomponents, i.e. inhibitory control (IC), cognitive flexibility (CF), and working memory (WM) [4] can be predicted from RSFC, GMV, and ReHo within this network in young and old adults**

Methods

- The eEFN comprised three **meta-analytically defined networks** reflecting CF [5], IC [6], and WM [7] as well as **sensorimotor networks**, to also include regions linked to input or output processing in typical EF-tasks
- Whole-brain imaging data of 138 younger (age range = 20-40 years, 82 females) and 116 older (age range = 60-80 years, 76 females) healthy adults were obtained from the enhanced Nathan Kline Institute-Rockland Sample (eNKI)
- We controlled for intracranial volume in the GMV and multimodal model
- **EF-related performance scores** provided in the eNKI dataset were used as behavioral target variables
- We performed **data reduction** via principal component scores for IC, CF, and WM abilities
- Individual z-transformed scores were then predicted from within-network RSFC, GMV, ReHo and the three modalities combined, using **partial least squares** with 100 repetitions of a 10-fold cross-validation scheme

Results

Meta-analytically defined extended EF-network



- Prediction accuracy of $r > .2$ is reported
- RSFC predicted IC performance ($\bar{r}=.24$; $\overline{MAE}=.45$) in the full sample
 - and WM performance in the younger subgroup ($\bar{r}=.21$, $\overline{MAE}=.55$)
- Regional GMV predicted IC and CF performance in the full sample ($\bar{r}\geq.35$; $\overline{MAE}\leq.41$)
 - IC and WM in the younger subgroup ($\bar{r}\geq.21$; $\overline{MAE}\leq.64$)
 - and CF in the older subgroup ($\bar{r}=.21$; $\overline{MAE}=.47$)
- ReHo predicted IC in the younger subgroup ($\bar{r}=.21$; $\overline{MAE}=.43$)
- The multimodal approach predicted CF and IC in the full sample ($\bar{r}\geq.28$; $\overline{MAE}\leq.42$)
 - and CF in the younger subgroup ($\bar{r}=.21$; $\overline{MAE}=.34$)

References

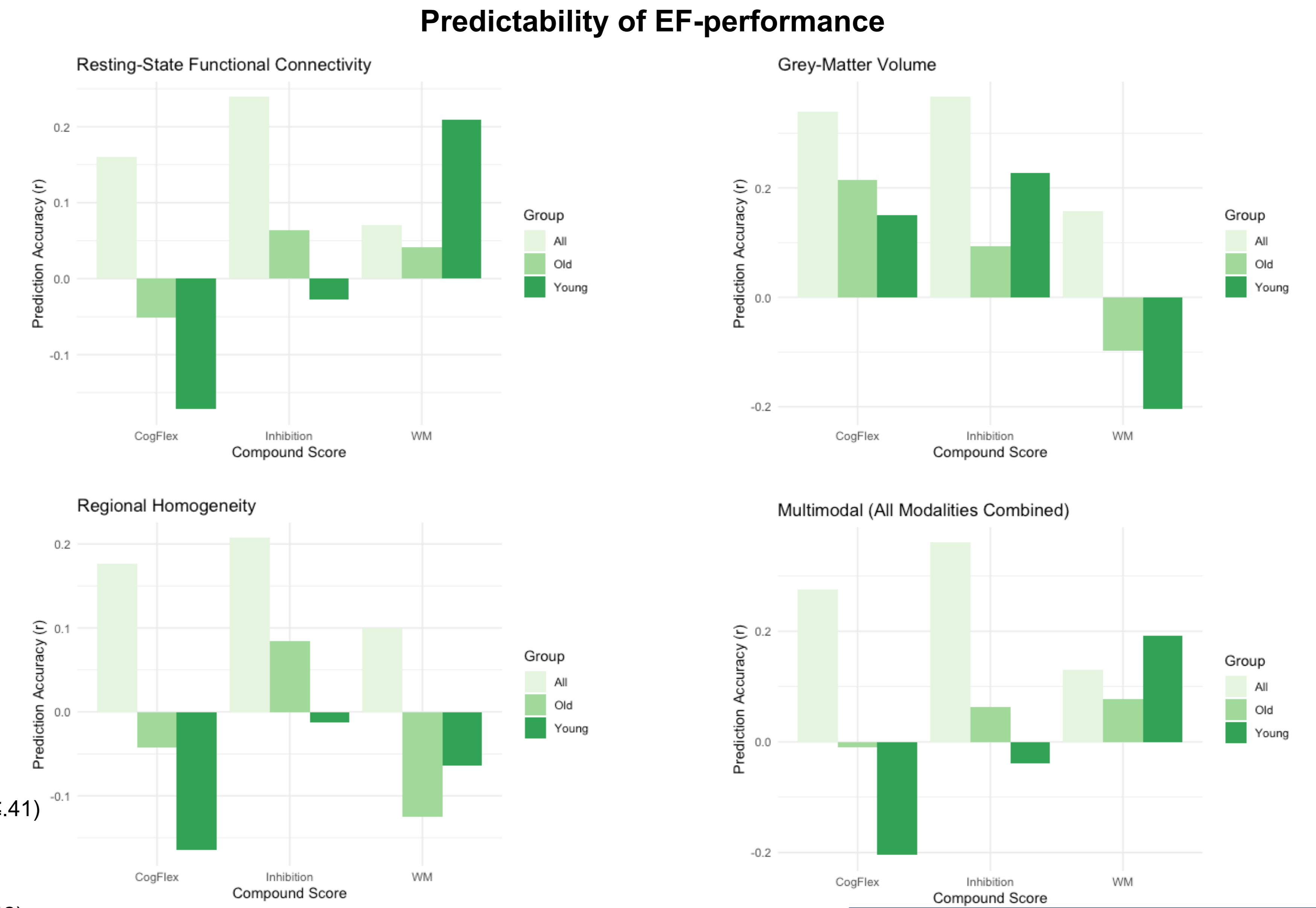
- [1] Langner, R., et al. (2015). Aging and response conflict solution: behavioural and functional connectivity changes, *Brain Structure and Function*, vol. 220, no. 3, pp. 1739-1757.
- [2] Steffener, J., et al. (2009). The Impact of Age-Related Changes on Working Memory Functional Activity, *Brain Imaging and Behavior*, vol. 3, no. 2, pp. 142-153.
- [3] Wu, T., et al. (2007). Normal aging decreases regional homogeneity of the motor areas in resting state, *Neuroscience Letters*, vol. 423, no. 3, pp. 189-193.
- [4] Alvarez, J. A., & Emory, E. (2006). Executive Function and the Frontal Lobes: A Meta-Analytic Review, *Neuropsychology Review*, vol. 16, no. 1, pp. 17-42.
- [5] 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, *Brain Structure and Function*, vol. 224, no. 5, pp. 1845-1869.
- [6] Cieslik, E. C., et al. (2015). Three key regions for supervisory attentional control: Evidence from neuroimaging meta-analyses, *Neuroscience & Biobehavioral Reviews*, vol. 48, pp. 363-375.
- [7] Rottschy, C., et al. (2012). Modelling neural correlates of working memory: A coordinate-based meta-analysis, *NeuroImage*, vol. 60, no. 1, pp. 830-846.

Acknowledgments

This study was supported by the Deutsche Forschungsgemeinschaft (DFG, EI 816/11-1), the National Institute of Mental Health (R01-MH074457), the Helmholtz Portfolio Theme "Supercomputing and Modeling for the Human Brain", the European Union's Horizon 2020 Research and Innovation Programme under Grant Agreement No. 720270 (HBP SGA1) and 785907 (HBP SGA2).

Discussion

- EF-performance prediction accuracy was generally rather low, but higher for eEFN regional GMV than network RSFC, ReHo, and the multimodal approach
- Our results raise the question if even a very comprehensive EF-network may **not be sufficient to capture the neural implementation of EFs**
- The findings suggest that **GMV may be a better predictor for EF-performance** compared to the other modalities
- Even the multimodal approach does not surpass regional GMV's predictive power
- Our results bring into question **if executive functioning can or should be defined in a network**
- The overall low prediction accuracy raises the question **if individual differences in EF-performance even manifest in canonical networks**, i.e. the recruitment of these networks might reflect executive processes but not the level of productivity



Conclusion

- **Our results show an overall low prediction accuracy for EF-performance which is higher for eEFN regional GMV than for network RSFC, ReHo, and the combined multimodal approach**
- **These findings question the predictability of EF-performance with the modalities used and call for further investigations testing more modalities**