A low-dimensional connectome manifold governs the organization and plasticity of social brain functions in humans

Sofie L Valk[1,2]; Philipp Kanske[3,4]; Bo-yong Park[5]; Seok-Jun Hong[6-8]; Anne Böckler-Raettig[9]; Fynn-Mathis Trautwein[10]; Boris C. Bernhardt[5]*, Tania Singer[11]*

1. Otto Hahn Group Cognitive Neurogenetics, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany; 2. INM-7, FZ Jülich, Jülich, Germany; 3. Clinical Psychology and Behavioral Neuroscience, Faculty of Psychology, Technische Universität Dresden, Dresden, Germany; 4. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany; 5. Multimodal Imaging and Connectome Analysis Lab, McConnell Brain Imaging Centre, Montreal Neurological Institute and Hospital, McGill University, Montreal, Quebec, Canada; 6. Center for the Developing Brain, Child Mind Institute, NY, USA; 7. Center for Neuroscience Imaging Research, Institute for Basic Science, Suwon, South Korea; 8. Department of Biomedical Engineering, Sungkyunkwan University, Suwon, South Korea; 9. Department of Psychology, Leibniz University Hannover, Germany; 10. Klinik für Psychosomatische Medizin und Psychotherapie, Universitäts Klinikum Freiburg, Freiburg, Germany; 11. Social Neuroscience Lab, Max Planck Society, Berlin, Germany

valk@cbs.mpg.de, *twitter: @sofievalk*

MAX-PLANCK-INSTITUT FÜR KOGNITIONS- UND NEUROWISSENSCHAFTEN

JÜLICH Forschungszentrum

Introduction

Social skills such as our abilities to understand feelings and thoughts are at the core of what makes us human. Current evidence suggests that (i) the neural basis of social capacities can be divided into multiple sub-systems; (ii) specific social and cognitive functions are likely facilitated by the segregation and integration of different brain systems depending on the task at hand; (iii) large-scale gradients reflect overarching organizational motifs of brain function. However, the exact relationship between specific social capacities and large-scale functional organization remains unclear.

Our study sought to directly examine the intrinsic relationship between social skills and functional topology using a combination of cross-sectional and longitudinal approaches.

Methods

We analyzed behavioral as well as task-based and task-free fMRI data from a large-scale mental training intervention, the *ReSource Project* (Singer, 2016) For further details, please see http://resource-project.org.

We derived task-based fMRI activation patterns associated with (i) attention based on a Cued-flanker task (Trautwein, 2016), (ii) socio-affective functions, such as empathy and compassion, based on the affect contrast in the EmpaTom task (Kanske, 2016), and (iii) socio-cognitive functioning, based on the ToM contrast of the EmpaTom task (Kanske, 2016)

To identify the manifold signatures of these networks, we applied non-linear dimensionality reduction to vertex-level resting-state functional MRI connectomes based on our open access software (Vos de Wael, 2020). These techniques identify a series of eigenmodes that describe spatial variations in connectivity, so called connectivity gradients (Coifman, 2005). Gradients of each individual were aligned to a template based on the Human Connectome Project dataset (Van Essen, 2020)

For each vertex, we calculated the Euclidian distance from the centre of the low-dimensional gradient manifold for each individual – creating a single *eccentricity* score, reflecting local network integration/segregation – as done recently (Bethlehem, 2020; Park, 2020). In addition we computed clustering coefficient and path length as alternative measures of integration and segregation (BCT toolbox; Rubinov, 2012) to validate our approach.

To study longitudinal change follow domain-specific social mental training, participants were randomly assigned to two training cohorts (TC1, N=80; TC2, N=81) who underwent three distinct and subsequent 3-months training modules (Presence, Affect, Perspective) with weekly-instructed group sessions and daily exercises, completed via cell-phone and internet platforms (**Figure 1**). Longitudinal changes in manifold eccentricity were assessed using mixed-effects analysis

Summary

All participants were followed with repeated multimodal neuroimaging and behavioral testing. Longitudinal analyses of functional networks indicated marked and specific reorganization following mental training. Socio-cognitive training resulting in an increased integration of multiple demand and default mode regions whereas attention-mindfulness resulted in their segregation. Socio-affective training resulted in an increased functional integration of ventral attention network with these regions along the principal gradient.
Changes in functional network organization were robust after varying analysis parameters, and predictive of change in behavioral markers of compassion and perspective-taking.

Thus, our longitudinal findings show that social brain networks can be reconfigured following social mental training in adults and that these changes result in behavioral change. These findings could inform the development and implementation of targeted training interventions aiming at cultivating social understanding and prosocial behavior.

Fig 1. Changes of functional integration and segregation following social mental training

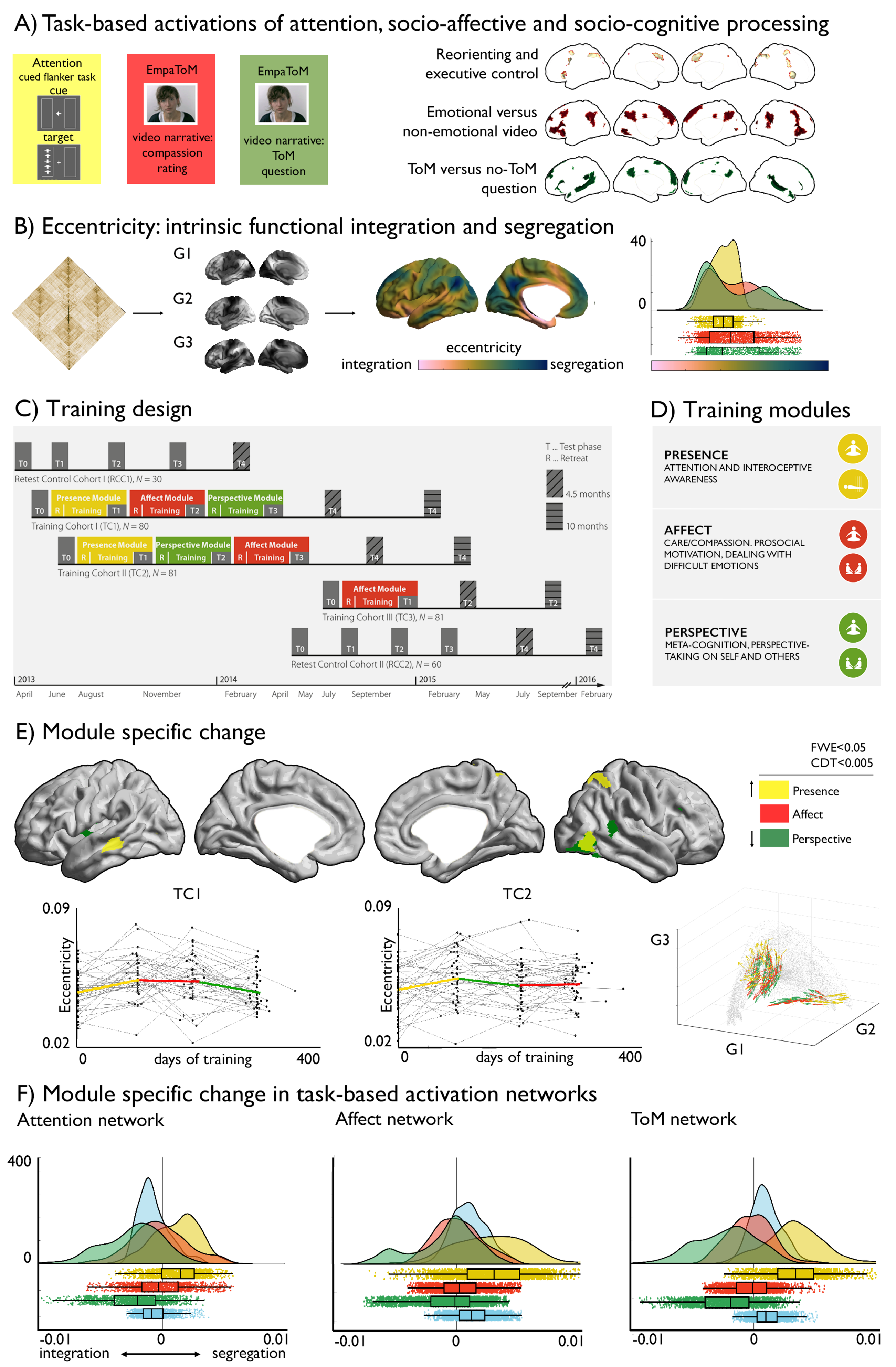


Fig 2. Changes along the principal functional gradient following social mental training

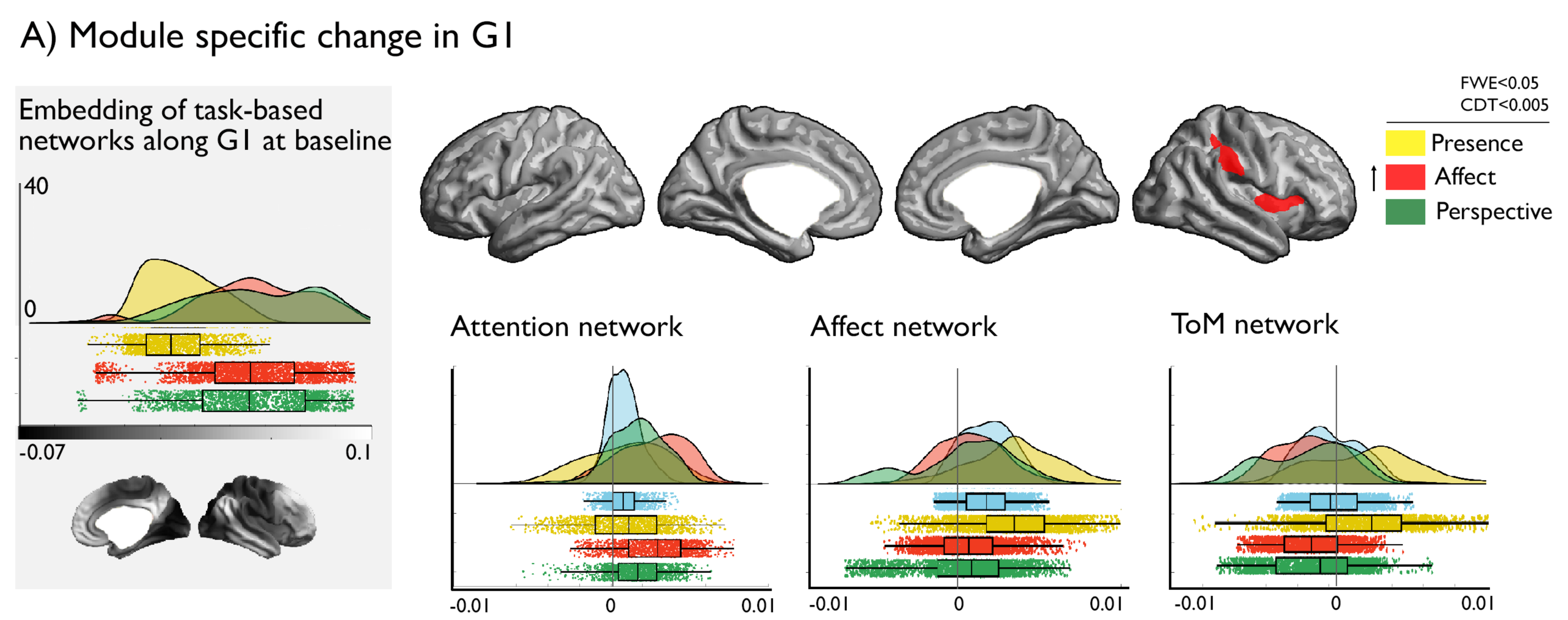
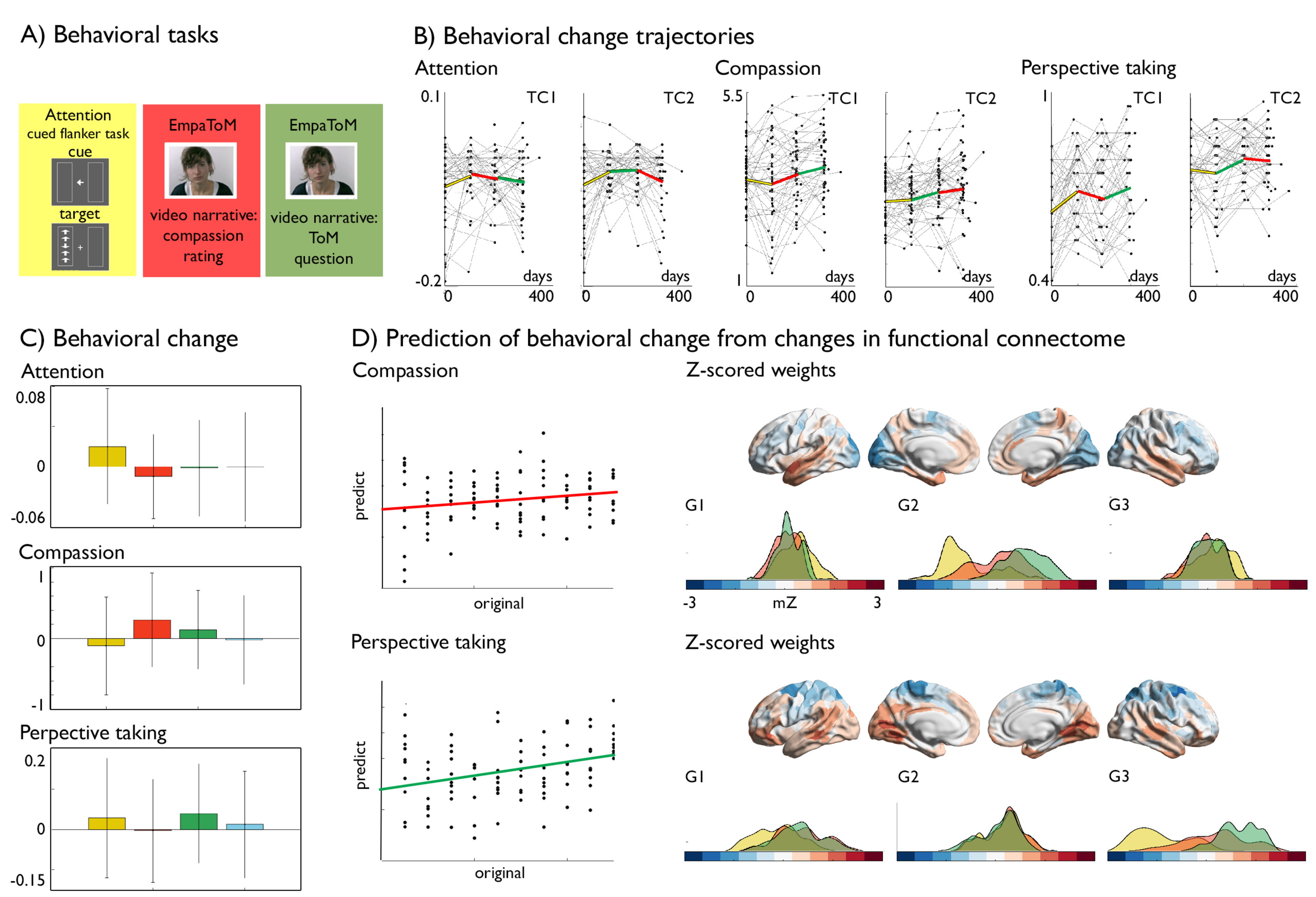
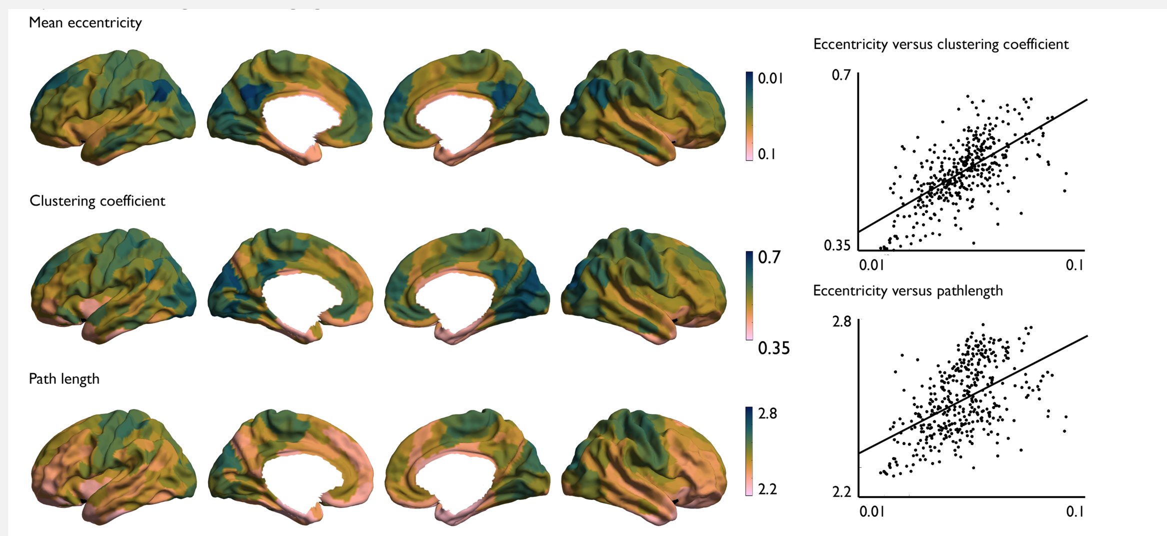


Fig 3. Prediction of behavioral change from training-induced changes along axis of functional organisation



Bonus: Eccentricity across approaches



References

Bethlehem, R. A. I., Paquola, C., Seidlitz, J., Ronan, L., Bernhardt, B. C., Consortium, C.-C., & Tsvetanov, K. A. (2020). Dispersion of functional gradients across the lifespan. *NeuroImage*

Coifman, R. R., Lafon, S., Lee, A. B., Maggioni, M., Nadler, B., Warner, F., & Zucker, S. W. (2005). Geometric diffusions as a tool for harmonic analysis and structure definition of data: diffusion maps. *Proc Natl Acad Sci U S A, 102*(21), 7426-7431. doi:10.1073/pnas.0500334102

Kanske, P., Bockler, A., Trautwein, F. M., & Singer, T. (2015). Dissecting the social brain: Introducing the EmpaToM to reveal distinct neural networks and brain-behavior relations for empathy and Theory of Mind. *Neuroimage, 122*, 6-19. doi:10.1016/j.neuroimage.2015.07.082

Margulies, D. S., Ghosh, S. S., Goulas, A., Falkiewicz, M., Huntenburg, J. M., Langs, G., . . . Smallwood, J. (2016). Situating the default-mode network along a principal gradient of macroscale cortical organization. *Proc Natl Acad Sci U S A, 113*(44), 12574-12579. doi:10.1073/pnas.1608282113

Park, B., Bethlehem, R. A. I., Paquola, C., Lariviere, S., Cruces, R. R., Vos De Wael, R., . . . Bernhardt, B. C. (2020). Macroscale connectome manifold expansion in adolescence. *bioRxiv*

Singer, T., Kok, B. E., Bornemann, B., Zurborg, S., Bolz, M., & Bochow, C. A. (2016). *The ReSource Project. Background, design, samples and measurements (2nd ed).*

Trautwein, F. M., Singer, T., & Kanske, P. (2016). Stimulus-Driven Reorienting Impairs Executive Control of Attention: Evidence for a Common Bottleneck in Anterior Insula. *Cereb Cortex*. doi:10.1093/cercor/bhw225

Van Essen, D. C., Smith, S. M., Barch, D. M., Behrens, T. E., Yacoub, E., Ugurbil, K., & Consortium, W. U.-M. H. (2013). The WU-Minn Human Connectome Project: an overview. *Neuroimage, 80*, 62-79. doi:10.1016/j.neuroimage.2013.05.041

Vos de Wael, R., Benkarim, O., Paquola, C., Lariviere, S., Royer, J., Tavakol, S., . . . Bernhardt, B. C. (2020). BrainSpace: a toolbox for the analysis of macroscale gradients in neuroimaging and connectomics datasets. *Nat Commun Biology*.

Worsley, K., Taylor, J. E., Carbonell, F., Chung, M. K., Duerden, E., Bernhardt, B. C., . . . Evans, A. (2009). SurfStat: A Matlab toolbox for the statistical analysis of univariate and multivariate surface and volumetric data using linear mixed effect models and random field theory. *Neuroimage, S102*.

Preprint:https://www.biorxiv.org/content/10.1101/2020.11.11.377895v3

OHBM, 2020