CHANGING THE SOCIAL BRAIN: PLASTICITY ALONG MACRO-SCALE AXES OF FUNCTIONAL CONNECTIVITY FOLLOWING SOCIAL MENTAL TRAINING

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ABSTRACT

Despite the importance of our ability to understand the thoughts and feelings of others, the social brain remains incompletely understood. Here, we studied the plasticity of social brain function in healthy adults following the targeted training of attention-mindfulness, socio-affective, and socio-cognitive skills for 9 months. 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. Changes in functional network organization were robust after varying analysis parameters, and predictive of change in behavioral markers of compassion and perspective-taking. Our results advance the understanding of the social brain, describing its intrinsic functional organization and reorganization following mental training.

INTRODUCTION

Humans have unique social skills that enhance cooperation and survival (Dunbar, 1998; Ochsner and Lieberman, 2001). These social capacities can largely be divided into several components (Schurz et al., 2020a; Singer, 2006): Firstly, socio-affective (or emotional-motivational) abilities allow us to share feelings with others, and may give rise to compassion and prosocial motivation (Batson, 2009; de Vignemont and Singer, 2006; Eisenberg and Fabes, 1990). Secondly, a socio-cognitive system gains access to beliefs and intentions of others, a skill also referred to as Theory of Mind (ToM) or mentalizing (Frith and Frith, 2006; Saxe and Kanwisher, 2003; Singer, 2006). Finally, there is evidence for a role of attention, action observation, and mindfulness as important auxiliary functions of these social aptitudes, which underlie self-other distinctions and awareness (Craig, 2009; Kleckner et al., 2017; Tomasello, 1995). Together, these human capacities combine externally and internally oriented cognitive and affective processes and reflect both focused and ongoing thought processes (Barrett, 2017; Chun et al., 2011; Murphy et al., 2019; Sormaz et al., 2018; Turnbull et al., 2020). However, to what extent these processes are malleable following targeted training is incompletely understood.

Previous functional neuroimaging studies have identified dissociable brain networks involved in these components of social cognition, which somewhat recapitulate large-scale functional networks also seen in the resting brain, notably the ventral attention network (VAN) and paralimbic networks in the case of socio-affective processing (Alcala-Lopez et al., 2018; Lamm et al., 2011; Schurz et al., 2020a), the default mode network (DMN) in the case of ToM (Alcala-Lopez et al., 2018; Schurz et al., 2020a), and multiple demand network (MDN) in the case of attention and action observation (Assem et al., 2020; Schurz et al., 2020a). Indeed, tasks probing empathy consistently elicit functional activations in anterior insula, supramarginal gyrus, and midcingulate cortex (Singer, 2006; Singer and Lamm, 2009; Singer et al., 2004), while ToM paradigms activate the DMN regions such as medial frontal cortex, temporo-parietal junction, and superior temporal sulcus (Bzdok et al., 2012; Saxe and Kanwisher, 2003; Schurz et al., 2020a). Conversely, attention and action observation activate inferior parietal and lateral frontal and anterior insular cortices (Corbetta et al., 2008; Corbetta and Shulman, 2002; Trautwein et al., 2016). At the same time, it has been shown that the capacity to understand the feelings and thoughts of others in naturalistic settings are supported by multiple processes and consequently implicate combinations of distributed brain networks (Alcala-Lopez et al., 2018; Chang et al., 2015; Pessoa, 2014; Raz et al., 2016; Schaafsma et al., 2015; Schilbach et al., 2013; Schurz et al., 2020b; Zaki et al., 2009). Thus, social cognitive processing can be understood as a hierarchical phenomenon, including automatic and controlled functional processes (de Waal, 2012; Preston and de Waal, 2002; Schurz et al., 2020b; Singer, 2006). However, a causal relationship between brain function and differentiable processes underlying social behavior has not been investigated.

Expanding cross-sectional association studies, longitudinal investigations can reveal links between social skills and the human brain, for example by targeted mental training designs. Only few previous studies have addressed longitudinal mental training effects in the domain of social cognition. While these have generally suggested changes in behaviour and MRI-based measures of brain structure and function (Pernet et al., 2021; Tang et al., 2015), sample

sizes were relatively modest and training intervals short. Moreover, few studies have compared different practices or focussed on different social skills specifically. Our work was realized in the context of the *ReSource* study (Singer et al., 2016), a large-scale study involved a targeted training of attention-mindfulness (*Presence* module), followed by socio-affective (*Affect* module) and socio-cognitive/ToM training (*Perspective* module) over the course of nine months. Whereas *Presence* aimed at initially stabilizing the mind and nurturing introspective abilities, the *Affect* and *Perspective* modules focussed on nurturing social skills such as empathy, compassion, and perspective taking on self and others. Based on the *ReSource* sample, our group could previously show differentiable change in cortical thickness following these modules, illustrating structural plasticity of the social brain (Valk et al., 2017). However, it remains unknown how targeted training of interoceptive and attentional processes, socio-affective competences, and socio-cognitive skills relative to changes in brain functional organization.

The overlap between functional activation patterns during specific social cognition paradigms and large-scale functional systems at rest implicates that these functional processes are underpinned by the intrinsic organization of the cerebral cortex (Mesulam, 1998). This organisation enables the spatial integrating and segregating of different cortical networks, and has been increasingly conceptualized to run along continuous dimensions, also referred to as connectivity gradients (Huntenburg et al., 2018; Margulies et al., 2016; Murphy et al., 2019; Paquola et al., 2019). Reliably identifiable from resting-state functional connectivity data, such gradients can be used to compactly describe neural organization (Haak and Beckmann, 2020; Haak et al., 2018; Hong et al., 2020; Margulies et al., 2016; Shine et al., 2019). For example, the principal gradient places transmodal association networks such as the DMN and paralimbic networks at a maximal distance from sensory and motor regions (Huntenburg et al., 2018; Margulies et al., 2016; Murphy et al., 2019). This segregation may allow association cortices to take on functions only loosely constrained by the environment, which likely facilitates the formation of abstract representations and transformations required for socio-cognitive and socio-affective processing (Smallwood et al., 2021). Complementing this sensory-transmodal hierarchy, the second gradient reflects a visual-somatomotor differentiation and the third gradient differentiates the MDN from the rest of the brain (Turnbull et al., 2020). Social processes likely have a differential positioning along these gradients, with ToM possibly being associated with transmodal networks such as the DMN (Margulies et al., 2016). Attention may reflect more external focus (Murphy et al., 2019), whereas socio-affective processes may include both alerting, emotionally salient, stimuli from the environment, and more abstract forms of ongoing thought and emotions (Schurz et al., 2020b). Effective connectivity studies in social cognition have furthermore shown that, depending on the task, different transmodal brain networks are either integrated and segregated (Barrett and Satpute, 2013; Betzel et al., 2016; Dajani and Uddin, 2015; Schurz et al., 2020a; Shine et al., 2019). For example, complex and demanding ToM tasks often involve an integration of distributed brain networks, such as the DMN and frontal parietal network (Schurz et al., 2020a; Shine et al., 2016). Conversely, segregation of brain networks may relate to a temporally and hierarchically reduced depth of processing, and may potentially be at play during attentional processes (Finc et al., 2020; Shine and Poldrack, 2018). However,

the precise mapping of social brain functions to intrinsic organizational axes is not understood to date.

Capitalizing on the longitudinal *Resource* study (Singer et al., 2016), here we studied functional network plasticity of the social brain. In particular (Singer et al., 2016), we examined functional network reorganization following the three training modules *i.e.*, *Presence* (promoting attention and interoceptive awareness, resembling mindfulness-based interventions (Kabat-Zinn, 1990)), *Affect* (focusing on socio-affective capacities, such as compassion, gratitude, dealing with difficult emotions), and *Perspective* (focusing on socio-cognitive skills, such as perspective-taking on self and others/ToM as well as metacognition). We sought to specifically assess plasticity of task-based functional networks contributing to attention, socio-affective, and socio-cognitive skills (Kanske et al., 2015; Trautwein et al., 2016) in an intrinsic coordinate system spanned by the first three functional connectivity gradients, together describing functional network integration and segregation. We hypothesized that the training of these social skills would result in dissociable functional reorganization. In addition to assessing the reorganization of brain functional architecture, we assessed associations to behavioral change in attention, compassion, and ToM markers using machine learning with cross-validation. A series of additional analyses evaluated the robustness of our findings with respect to analysis parameter choices and further contextualized findings.

RESULTS

Changes in functional eccentricity following the targeted training of social skills

We analyzed resting-state as well as task-based fMRI and behavioral data from a large-scale mental training intervention, the *ReSource Project* (Singer et al., 2016). For details, see http://resource-project.org and the preregistered trial https://clinicaltrials.gov/ct2/show/NCT01833104.

We first derived task-based fMRI activation patterns associated with (i) attention, based on a Cued-flanker task (Trautwein et al., 2016), (ii) socio-affective functions, such as empathy and compassion, based on the affect contrast in the EmpaTom task (Kanske et al., 2015), and (iii) socio-cognitive functioning, based on the ToM contrast of the EmpaTom (Kanske et al., 2015) in the current sample. These networks describe differentiable combinations of functional communities associated with attention, socio-emotional, and socio-cognitive task-activations, including MDN, ventral attention network (VAN), and DMN (**Supplementary Results**). To compactly describe large-scale functional brain organization, we reduced the dimensionality of the resting-state fMRI connectomes using previously utilized techniques (Vos de Wael et al., 2020). The identified eigenvectors are spatial gradients describing continuous axes of connectivity space (Coifman et al., 2005; Margulies et al., 2016; Vos de Wael et al., 2020). Gradients of each individual were aligned to a template based on the Human Connectome Project dataset (Van Essen et al., 2013; Vos de Wael et al., 2020). For each vertex, we calculated its distance from the center of the gradient coordinate system formed by G1, G2, and G3 for each individual. This eccentricity captured vertex-wise intrinsic functional integration (low eccentricity) and segregation (high eccentricity) in a single scalar value (Bethlehem et al., 2020; Coifman et al., 2005; Park et al., 2020). Eccentricity indeed correlated positively ($r>0.5$, $p<0.001$ when controlling for spatial autocorrelation) with network clustering coefficient and characteristic path length, supporting that it captured segregation and integration of large-scale networks (**Supplementary Results**). Highest segregation was observed in visual and sensory-motor networks, while ventral attention and limbic networks were closest to the center of the space (Menon and Uddin, 2010). Calculating eccentricity scores of the activations at baseline (**Figure 1C**), attention networks had a lower eccentricity than both social networks (both $p<0.001$).

We then examined how functional organization of the different social networks changed following their targeted training. *Resource* participants were randomly assigned to two training cohorts (TC1, N=80; TC2, N=81) and underwent a 9-month training consisting of three sequential training modules with weekly group sessions and daily exercises, completed via cell-phone and internet platforms (**Figure 1, Table 1-3,** *Materials and Methods and Supplementary Materials for more details*). TC1 and TC2 underwent the latter two modules in different order (TC1: *Affect→Perspective*; TC2 *Perspective→Affect*) to serve as active control groups for each other (**Figure 1C**). Additionally, a matched test-retest control cohort did not undergo any training (RCC, N=90), but was followed with the same measures as TC1 and TC2, as well as an active control group (TC3; N=81 completed three months of *Affect* training only). All participants were measured at the end of each three-month module (T_1, T_2, T_3) using 3T MRI and behavioral measures that were identical to the baseline (T_0) measures**.**

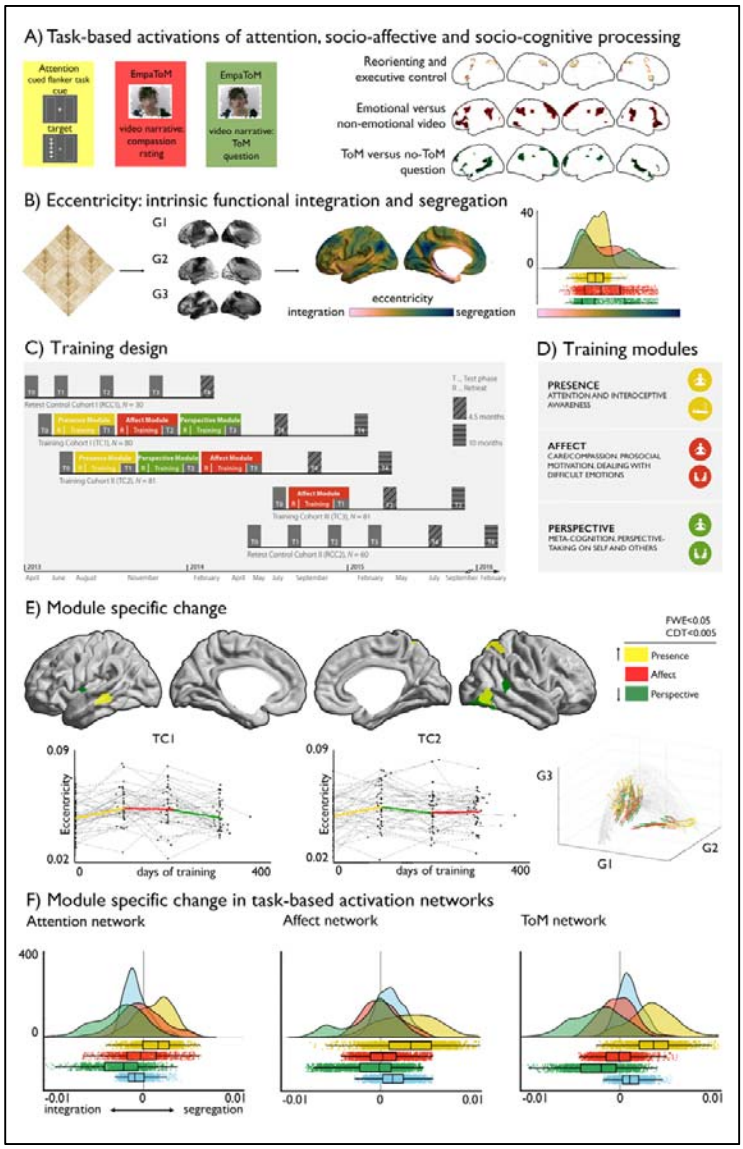

Figure 1. Functional eccentricity alterations of the social brain following mental training. A). Functional localizers (Kanske et al., 2015; Trautwein et al., 2016) and their mappings projected on the cortex**; B**) Vertex-level eccentricity from rs-fMRI by combining the first three gradients (G1-G3); *middle*: vertex-wise eccentricity and *right*: eccentricity of task-based social networks; **C**). Training design of the *ReSource* study; **D**). Training modules; **E**). *upper panel:* Differential change in 3D gradient distance following mental training, *lower panel left:* Average change in overlapping clusters associated with eccentricity change in *Presence* and *Perspective* (light green) following *Presence* (yellow), *Affect* (red), and *Perspective* (green) in TC1 and TC2; *lower panel right*: visualization of local eccentricity changes as a function of 3d gradient space. Arrows indicate direction of change; **F**). Changes in average network eccentricity, colored by training: *Presence* (yellow), *Affect* (red), *Perspective* (green), and *retest controls* (light blue). Whole brain findings are corrected for multiple comparisons at $p_{FWE}<0.005$, two-tailed.

Our main analysis tracked longitudinal change in functional eccentricity and each gradient separately (G1-G3) using mixed-effects models (Dale et al., 1999). We observed marked eccentricity changes following *Presence* and *Perspective*. *Presence* training resulted in increased eccentricity of bilateral temporal and right superior parietal areas (family-wise error corrected p-value, $p_{FWE}<0.05$), indicating increased segregation of these regions. *Perspective* training resulted in decreased eccentricity of right temporal regions, together with left insular

cortices (p_{FWE}<0.05). We observed no significant eccentricity change following *Affect* training. Trajectories were similar in TC1 and TC2 (**Figure S2**).

Following, we evaluated training-related alterations in the task-derived functional networks. We observed increases in eccentricity of the attention (t=2.43, p=0.05) and socio-cognitive network (t= 3.24, p=0.01) in following *Presence* training, whereas both the attention (t=-2.42, p=0.05) and socio-cognitive network (t=-2.91, p=0.02) showed decreased eccentricity following *Perspective* training (**Figure 2D**). These findings indicated that functional connectivity within task-based attention and socio-cognitive network becomes more dissimilar from other networks following the training of mindfulness-attention during *Presence* training, whereas the training of socio-cognitive skills during *Perspective* leads to increased similarity of attention and socio-cognitive networks with the rest of the connectome. Post-hoc analysis confirmed that eccentricity changes in task-based functional networks were comparable within TC1 and TC2 separately (**Figure S2**), relative to RCC (**Figure S3**) and when controlling for global signal (**Figure S4**). Studying changes within large-scale functional communities (Yeo et al., 2011), we found similar patterns indicating differentiable shifts in integration and segregation after *Presence* and *Perspective* training (**Supplementary Results**).

Relation to alterations in connectome gradient embedding

Having established changes in overall patterns of segregation and integration following *ReSource* training, we studied alterations within the first three large-scale gradients (**Figure 2**).

As in prior work (Margulies et al., 2016), the first gradient (G1) differentiated sensory-motor from transmodal systems, such as the default mode network (DMN). At baseline, attention networks had a lower position relative to both socio-affective (p<0.001) and socio-cognitive (p<0.001) networks. The two latter networks both occupied the transmodal end of G1. Within G1, we found increases after *Affect* along G1 in right supramarginal gyrus and right middle insula (p_{FWE}<0.05).

The second gradient (G2) ran from sensory-motor to visual networks. For G2, attention networks were lower than socio-affective networks (p<0.003), but higher than socio-cognitive networks (p<0.001). Socio-affective networks were at a higher position on G2 relative to socio-cognitive networks (p<0.001). Studying alterations following mental training along G2, we found decreases in right posterior insula extending to superior temporal gyrus(p_{FWE}<0.05) following *Presence* and decreases in right orbitofrontal cortex (p_{FWE}<0.05) following *Perspective*.

The third gradient (G3) differentiated the multiple-demand network, MDN (Duncan, 2010), from the rest of the brain. For G3, attention networks had a higher loading than socio-affective networks (p<0.001), which, in turn, had a higher loading than socio-cognitive networks (p<0.001), indicating a clear differentiation of all three networks along this gradient. Within G3, we observed decreases in left inferior temporal and occipital regions (p_{FWE}<0.001) following *Affect*. We did not observe significant change in task-based networks along gradient 1-3. Repeating analysis in both training groups separately, indicated particularly whole brain

changes in *Affect* along G1 were consistently observed in both cohorts (**Supplementary Results**).

In sum, we could show consistent and divergent functional network plasticity of key regions in the MDN, VAN, and DMN following the training of attention-mindfulness, socio-affect and socio-cognition.

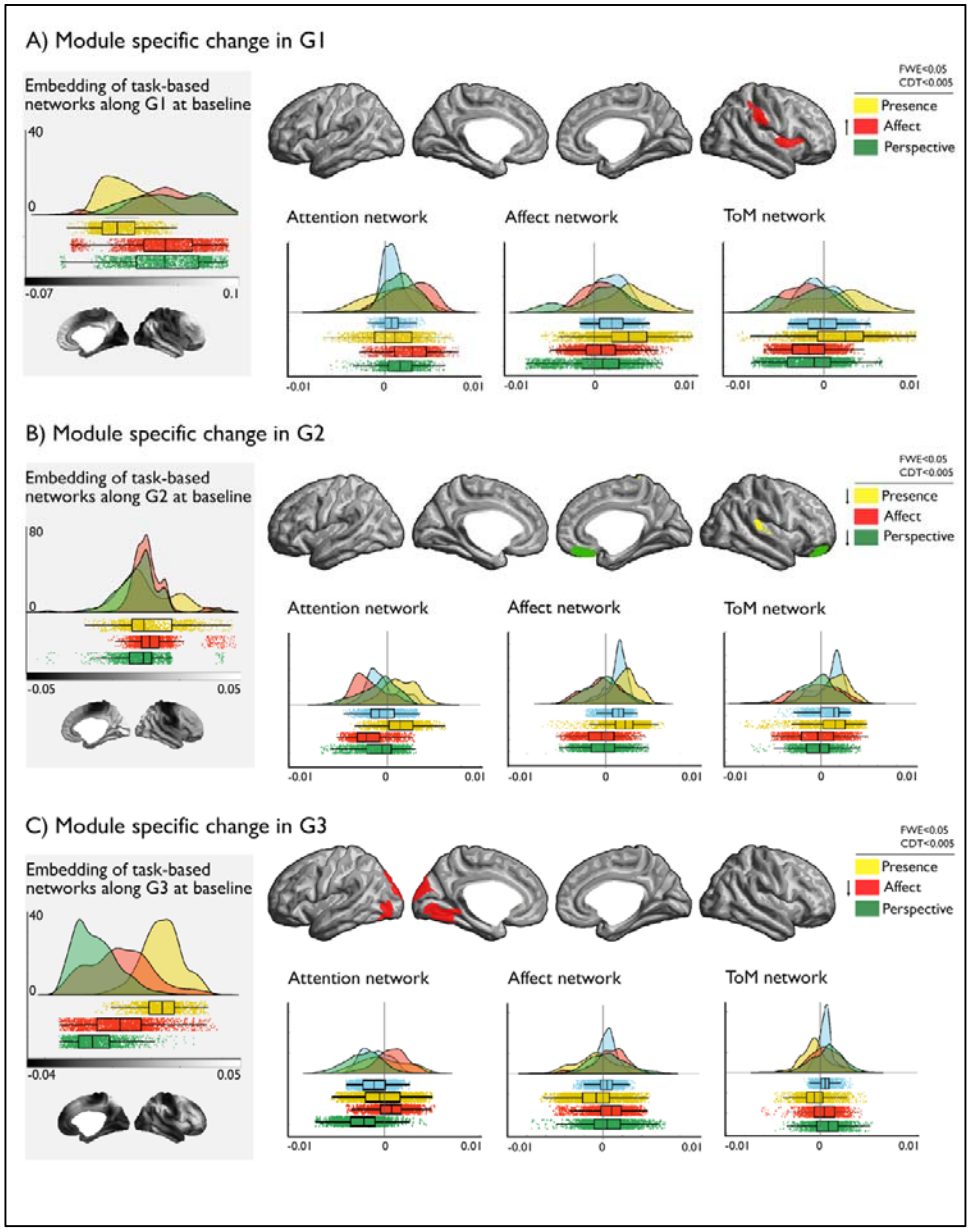

Figure 2. Functional gradient alterations of the social brain following mental training. A-C) *Left panel (grey):* Embedding of task-based networks along G1-G3. *upper panel*: Changes in G1-G3 respectively, arrows in the panel next to the color-boxed indicate increase of decrease; *lower panel*: visualization of task-based network-specific changes in each gradient. Colors indicate the training module (yellow=*Presence*; red=*Affect*; green=*Perspective*) and *retest controls* (light blue). Whole brain findings are corrected for multiple comparisons at $p_{FWE}<0.005$, two-tailed.

Associations between functional network reconfiguration and behavioral change

Last, we evaluated whether the above alterations in functional eccentricity following mental training could predict behavioral changes following the *Resource* training. We first replicated previous observations of module-specific behavioral change (Trautwein et al., 2020) in the current sample with fMRI data available. Attention scores increased during *Presence* relative to the other modules (t=3.837, p<0.001) and to RCC (t=3.193, p<0.001). Compassion scores increased following *Affect* relative to the other modules (t=3.361, p<0.001) and to RCC (t=3.695, p<0.001). Finally, ToM scores were marginally increased during *Perspective* relative to the other modules (t=1.600, p=0.055) and RCC (t=1.588, p=0.056).

Supervised learning (elastic net, 10 components, 5-fold cross validation, 5000 repetitions (Chang et al., 2015)) was utilized to predict behavioral change from the three gradients combined. G1-G3 combined could predict compassion (prediction – outcome r=0.20, mean absolute error (MAE): 2.44, p=0.046) and ToM scores (r=0.24, MAE:2.36, p=0.02) change. Binning change scores in 10 bins improved predictions relative to using the raw change scores in both compassion and ToM, yet change in attention was not predictable (r=-0.03) (**Supplementary Results**). Features were selected in anterior and inferior temporal, limbic, and visual cortex, and related predominantly to G2 for compassion, particularly with lower weights on attention and higher weights on socio-cognitive networks. Conversely, features predictive of ToM change related to a dissociable pattern between attention and socio-cognitive network weights in G3.

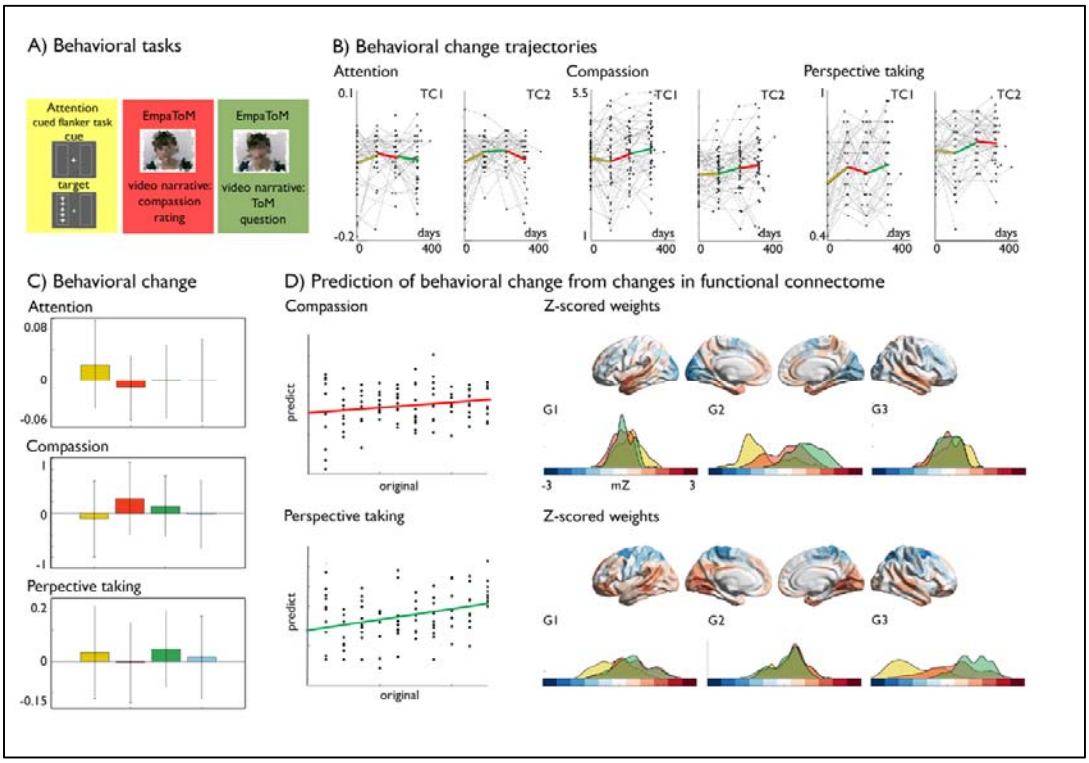

Figure 3. Association between changes in functional embedding and changes in behaviour. A). Behavioral tasks that measured attention, compassion, and perspective-taking; **B**). Behavioral measurements in TC1 and TC2 across time-points (Trautwein et al., 2020); **C**). Behavioral change across modules; **D**). Prediction behavior change across time-points. *left:* scatter of predicted versus original scores; *right upper:* average bootstrapped z-score; *right lower:* average bootstrapped z-score within task-based network per gradient dimension.

Robustness analyses

Various additional analysis indicated robustness of our findings (**Supplementary Results**);

- To validate our vertex-level approach, we additionally computed network-level index of segregation and integration; the *dispersion* within as well as *distance* between task-based fMRI activations in 3D gradient space (Bethlehem et al., 2020), respectively reflective of segregation within and between networks. Using these network-level metrics we observed similar patterns of network integration and segregation following the mental training modules.
- Taking a graph theoretical approach to integration and segregation, using clustering coefficient and path length (Rubinov and Sporns, 2010), we could confirm differentiable patterns of integration and segregation in task-based functional networks after *Presence* and *Perspective* modules.
- We observed similar results when performing global signal regression, indicating the observed patterns of intrinsic functional integration and segregation did not relate to global signal changes as a function of training.
- We observed no significant association with change in task-unrelated thoughts when evaluating change in post-scan thought probes after each mental training block, suggesting the contents of thought during resting state assessment did not systematically vary as a function of mental training.
- As the task-based activations within the current sample were key to our analysis, we performed extensive decoding to leverage the dissociability of the functional activations associated with attention, socio-affect, and socio-cognitive tasks in the present sample with canonical functional-networks, transcriptomic expression, and meta-analytical task space. These measures provide further contextualization of our sample specific networks, and as such help to interpret the sample and metric-specific networks. These additional analyses confirmed the observed task-based networks were consistently different across samples and approaches.

DISCUSSION

Assessing longitudinal change following mental training provided evidence for the interrelation of intrinsic functional brain organization and social and attentional functions. Particularly, our findings show functional segregation of regions in the multiple demand network (MDN) and default mode network (DMN) following *Presence* training, indicating that these networks differentiated from the rest of the cortex. Conversely, *Perspective* training resulted in their functional integration. *Affect* resulted in marked alterations of functional organization of regions in the ventral attention network (VAN) along the first gradient specifically, reflecting an increased integration of these regions with MDN and DMN networks. Second, we could predict changes in compassion and ToM scores based on co-occurring changes in large-scale functional organization, suggesting behavioral relevance of functional network alterations following mental training. In sum, our study showed that the concerted training of social skills results in dissociable changes in the functional connectome. Although our work focused on healthy adults ranging from 20 to 55 years of age, our findings overall support the possibility that targeted mental training can enhance social skills and lead to co-occurring functional network reconfigurations. These findings could inform future efforts to develop interventions aimed at cultivating the understanding of thoughts and feelings of others.

Higher cognition reflects a balance between parallel processing in an integrated architecture versus more segregated hierarchical processing (Bertolero et al., 2015; Mesulam, 1998; Schurz et al., 2020a; Schurz et al., 2020b). Analyzing task-derived fMRI networks involved in social and attentional processes at baseline, we could show that these networks were positioned differently in a coordinate system spanned by the first three functional gradients. Echoing prior work in young adults (Margulies et al., 2016), the principal gradient ran from unimodal to transmodal systems such as the DMN. This axes aligns with classic notions of cortical hierarchy (Margulies et al., 2016), axes of microstructural differentiation (Huntenburg et al., 2017; Paquola et al., 2020b; Paquola et al., 2019) and cortical evolution, with heteromodal regions undergoing recent expansions in the human lineage (Valk et al., 2020; Xu et al., 2020). In our findings, socio-affective and socio-cognitive functional activations were located at the higher end of this functional hierarchy stretching from perception/action to flexible cognition. Functions key to social cognition such as ToM are often co-localized with, if not equal to, heteromodal association systems such as the DMN (Alcala-Lopez et al., 2018; Alcala-Lopez et al., 2019; Alves et al., 2019; Kernbach et al., 2018). The DMN is thought to integrate multiple streams of information (Margulies et al., 2016; Paquola et al., 2020a; Turnbull et al., 2020), coordinating internal and external information (Frith and Frith, 2003; Murphy et al., 2018; Murphy et al., 2019; Schurz et al., 2020b), and supporting predictive processing (Chanes and Barrett, 2016). Conversely, attention was associated with the middle of this axes, indicating its function to bridge sensory and integrative processing. Notably, task-based networks involved in attention, socio-affective, and socio-cognitive skills were linearly ordered along the third gradient, which dissociates the MDN from rest of the brain, with attention closest to the MDN and socio-cognitive skills closest to the DMN. Unlike the DMN, the MDN engages in preferentially in externally oriented tasks (Buckner et al., 2008; Margulies et al., 2016). Recent studies have shown that the third gradient furthermore differentiates socio-episodic memory processes in DMN from task-focused processing taking

place in the MDN (Turnbull et al., 2020; Turnbull et al., 2019a). The MDN, including fronto-parietal and dorsal attention networks, has been implicated in attention/executive function (Alcala-Lopez et al., 2018; Assem et al., 2020). Indeed, whereas task-based activations in perspective-taking showed overlap with the DMN, task-based activation associated with attention related to MDN. Conversely, socio-affective skills were found to be in the middle of the organizational axis dissociating MDN from DMN. This positioning of socio-affective task-based activations along the third gradient between attention and ToM may be reflective of a regulative role of functional activity of MDN and DMN (Menon and Uddin, 2010). As such, we could show that the task-based functional activations associated with attention, socio-affect and socio-cognition each were placed at unique locations along cardinal axes of functional organization, particularly those dissociating MDN from DMN and other cortical networks.

Studying functional network plasticity following *ReSource* training, we found that regions in both the MDN and DMN integrated further following *Perspective* training, whereas they segregated following *Presence*. In the context of social cognition, integrated states might reflect active thought processes such as those required when engaging in ToM, while more segregated states may reflect automation and domain-specific function (Finc et al., 2020). Mindfulness cultivated during *Presence* may reduce habitual thought patterns and enhance momentary awareness (Lutz et al., 2019) – possibly captured by functional network segregation. Corroborating these findings, *Presence* training shifted the socio-cognitive network along the principal gradient G1, indicating a segregation of this network from more perceptual/action driven modes of processing. Our observations in the domain of social skill training align with previous mental training studies in other domains; working memory task performance has been associated with decreased modularity (increased integration) whereas automation following working memory training was associated with increased modularity (segregation) of MDN and DMN (Finc et al., 2020). Second, mental training has been reported to result in reduced intra-network connectivity in the DMN, VAN and somatomotor networks, reflecting integration (Cotier et al., 2017). More generally, our findings may be in line with the Global Workspace Theory, which poses that automated tasks can be performed within segregated clusters of regions, whereas those that are novel and challenging require integration (Dehaene et al., 1998). Importantly, previous literature has indicated that functional brain networks are dominated by stable group and individual factors (Gratton et al., 2018). At the same time, functional activity is inherently dynamic, reflecting different cognitive states associated with faciliatory and inhibitory processing (Shine et al., 2018; Shine and Poldrack, 2018). Thus, it is likely that though each functional network has its place within large-scale functional organization, changes enabled by mental training reflect more dynamic elements of functional network organization. As such, our work expands pervious findings on region-specific effects (Tang et al., 2015) by providing a system-level perspective on how the social brain adaptively reconfigures following targeted, and multifaceted interventions.

We did not observe changes in eccentricity of task-based networks following the *Affect* training module. However, core nodes of the VAN, also referred to as saliency network (Uddin, 2015), such as the supramarginal gyrus and insula, shifted upwards along the

principal gradient G1, indicating that this network may more closely affiliate with the MDN and the DMN following this module. The VAN has been implicated in empathy (Lamm et al., 2011; Turnbull et al., 2019b), and may also contribute to the regulation of high-level cognitive processes and attention. Previous work has furthermore suggested VAN are part of the diverse club, a set of regions with high participation coefficients reflecting their diverse connectivity patterns supporting global integration (Bertolero et al., 2017). Its change may reflect a processing shift of the VAN towards a more integrative functional role. In addition, these regions are suggested to mediate the activity within fronto-parietal and DMN (Menon, 2015; Menon and Uddin, 2010). It is possible that the lack of change in eccentricity and increases of the VAN along G1 following socio-affective training reflects such a coordinating role (whereas its decreases following mindfulness attention result in lack of coordination and increased segregation). Such an interpretation aligns with theories of emotional allostasis, suggesting that affective processing may balance integration and segregation of brain function to regulate resources dynamically (Barrett, 2017; Chun et al., 2011). Notably, though the current work focused on cortical networks, it is likely also subcortical regions contribute to the functional organization of the social brain (Kanske et al., 2015; Shine, 2020). Follow-up work that studies plasticity of sub-cortical function and structure in the context of the social brain will provide additional system-level insights on the social brain.

Using supervised learning with cross-validation, we found behavioral markers of social functions to be associated with training-related reorganization in functional connectome axes. In particular, we could predict both compassion and perspective-taking change during the *Affect* and *Perspective* blocks. *Affect* training nurtured compassion, prosocial motivation, and emotional regulation, as reflected in the increases in compassion scores following the *Affect* module in particular. We observed that increased weights in temporal/limbic regions following *Affect* could predict compassion change. Previous work suggests compassion/positive affect is likely emotion-motivational systems (Klimecki et al., 2014) but also interoceptive information (Barrett, 2017), as supported by (para)limbic regions such as ventral anterior insula and parahippocampa regions (Barrett, 2017; Turnbull et al., 2020; Turnbull et al., 2019b). On the other hand, *Perspective* training focused on training perspective-taking of self and others and was associated with increases in ToM scores (Trautwein et al., 2020). Behavioral change in perspective-taking following *Perspective* could be predicted by positive weights in the DMN (which overlaps with the task-based ToM network), whereas the MDN (which overlaps with the task-based attention network) had decreased weights. This may reflect that increases in perspective-taking are supported by a dissociation of focussed, externally-oriented processes mediated by MDN function and DMN functions that increasingly integrate these with internally-oriented processing (Turnbull et al., 2020). These observations underscore the differentiation between socio-emotional and socio-cognitive processes, and provide evidence that change in compassion and perspective-taking is captured by change intrinsic functional reorganization at the level of the individual.

In sum, by combining cross-sectional with longitudinal approaches, we could show how different modules of social mental training resulted in changes in functional network organization. In line with prior work on the relationship between grey matter structure and the *ReSource* training in the same sample (Valk et al., 2017), our work shows intrinsic

separability of processes underlying social functions. Notably, our work, in part, relied on within-sample task-based activations associated with attention, socio-affective, and socio-cognitive domains and previous work indicates that functional activations in tasks probing social processes are variable as a function of task operationalization (Schurz et al., 2020a; Schurz et al., 2014; Schurz et al., 2020b). Indeed, though meta-analytical decoding showed all three tasks were associated with the probed functions based on the task-based neuroimaging literature, they additionally involved other processes such as inhibition, cognitive control and memory (Alcala-Lopez et al., 2019; Schurz et al., 2020a; Schurz et al., 2014; Schurz et al., 2020b). Moreover, task-based activations used in the current study could be associated with different transcriptomic patterns, replicating and expanding prior work linking task-based activations with transcriptomic organization (Hansen et al., 2021), suggesting they may reflect differentiable neurogenetic pathways. Taken together, the current work underscores the differentiation of processes underlying our ability of understand the thoughts and feelings of ourselves and others within the functional organization of the human brain, providing a system-level perspective on social functioning.

MATERIALS AND METHODS

Experimental design

Participants. A total of 332 healthy adults (197 women, mean±SD=40.7±9.2 years, 20-55 years), recruited in 2012-2014 participated in the study, see Table 1 for more details. More than 95% of our sample was Caucasian, with catchment areas balanced across two German municipalities (Berlin and Leipzig). Participant eligibility was determined through a multi-stage procedure that involved several screening and mental health questionnaires, together with a phone interview [for details, see (Singer et al., 2016)]. Next, a face-to-face mental health diagnostic interview with a trained clinical psychologist was scheduled. The interview included a computer-assisted German version of the Structured Clinical Interview for DSM-IV Axis-I disorders, SCID-I DIA-X (Wittchen and Pfister, 1997) and a personal interview, SCID-II, for Axis-II disorders (First et al., 1997; Wittchen et al., 1997). Participants were excluded if they fulfilled criteria for: i) an Axis-I disorder within the past two years; ii) Schizophrenia, psychotic disorders, bipolar disorder, substance dependency, or an Axis-II disorder at any time in their life. No participant had a history of neurological disorders or head trauma, based on an in-house self-report questionnaire used to screen all volunteers prior to imaging investigations. In addition, participants underwent a diagnostic radiological evaluation to rule out the presence of mass lesions (e.g., tumors, vascular malformations). All participants gave written informed consent and the study was approved by the Research Ethics Committees of the University of Leipzig (#376/12-ff) and Humboldt University in Berlin (#2013-02, 2013-29, 2014-10). The study was registered at ClinicalTrials.gov under the title "Plasticity of the Compassionate Brain" (#NCT01833104). For details on recruitment and sample selection, see the full cohort and study descriptor (Singer et al., 2016).

Study design. Our study focused on two training groups: training cohort 1 (TC1, n=80 at enrolment) and training cohort 2 (TC2, n=81 at enrolment), as well as a retest control cohort (RCC) that was partly measured prior to (n=30 at enrolment) and partly after (n=60 at enrolment) TC1 and TC2. A third training cohort (TC3, n=81 at enrolment) underwent an independent training program, and was included as an additional active control for the *Presence* module. Participants were selected from a larger pool of potential volunteers by bootstrapping without replacement, creating cohorts not differing significantly with respect to several demographic and self-report traits. Total training duration of TC1 and TC2 was 39 weeks (~nine months), divided into three modules: *Presence*, *Affect*, and *Perspective* (see below, for details), each lasting for 13 weeks (**Figure 1**). TC3 only participated in one 13-week *Affect* training, and is only included in supplementary robustness analyses, so that the main analysis of functional plasticity focusses on TC1 and TC2. Our main cohorts of interest, TC1 and TC2, underwent *Affect* and *Perspective* modules in different order to act as active control cohorts for each other. Specifically, TC1 underwent "*Presence-Affect-Perspective*", whereas TC2 underwent "*Presence-Perspective-Affect*". TC1, TC2, and RCC underwent four testing phases. The baseline-testing phase is called T0; testing phases at the end of the xth module are called Tx (*i.e.*, T1, T2, T3). In RCC, testing was carried out at similarly spaced intervals. The study had a slightly time-shifted design, where different groups started at different time points to simultaneously accommodate scanner and teacher availability. As we focused on training-related effects, we did not include analysis of a follow-up measurement

T4 that was carried out 4, 5, or 10 months after the official training had ended. For details on training and practice set-up, timeline, and measures, see (Singer et al., 2016).

Final sample. We excluded individuals with missing structural and/or functional MRI data and/or a framewise-displacement of >0.3mm (<5%) (Power et al., 2012) and individuals with gradients that showed less than r=0.5 correspondence to the average gradient patterns were disregarded for analysis (<1%), as recommended (Hong et al., 2020). Further details of sample size per time-point and exclusion criteria are in **Table 1-3**.

Table 1. Participant inclusion in resting-state analysis.

Recruited (N, mean age, % female)	T_0 (N)	T_1 (N)	T_2 (N)	T_3 (N)
Total (N = 332)	284	264	185	188
TC1 (N = 80; 41.3; 58.8)	72	66	56	55
TC2 (N = 81; 41.2; 59.3)	69	60	63	66
RCC (N =90; 40.0; 58.9)	72	71	66	67
TC3 (N = 81; 40.4; 60.5)	71	67		

Table 2. Reason for missing data across the study duration. *MR incidental findings* are based on T_0 radiological evaluations; participants who did not survive *MRI quality control* refers to movement and/or artefacts in the T1-weighted MRI; dropout details can be found in (Singer et al., 2016); *no MRT*: due to illness / scheduling issues / discomfort in scanner; *other*: non-disclosed; *functional MRI missing:* no complete functional MRI; *functional MRI quality:* >0.3mm movement (low quality in volume + surface)

Reason for dropout (TC1, TC2, RCC)	T_0	T_1	T_2	T_3
Structural MR incidental finding	5	(5 based on T_0)	(5 based on T_0)	(5 based on T_0)
Structural MRI quality control	7	6	4	2
Dropout	2	7(2 based on T_0)	7(9 based on T_{01})	7 (16 based on T_{012})
Medical reasons	1	7(1 based on T_0)	7(8 based on T_{01})	(15 based on T_{012})
Other	4	10	7	7
Functional MRI missing	4	10	11	4
Functional MRI quality	14 (26)	5(23)	8(14)	3(5)

Table 3. Reason for missing data across the study duration. *MR incidental findings* are based on T_0 radiological evaluations; participants who did not survive *MRI quality control* refers to movement and/or artefacts in the T1-weighted MRI; dropout details can be found in (Singer et al., 2016); *no MRT*: due to illness / scheduling issues / discomfort in scanner; *other*: non-disclosed.

Reason for dropout (TC3)	T_0	T_1
MR incidental finding	3	(3 based on T_0)
MRI quality control	0	0
Dropout	0	3
Medical reasons	1	2
Other	5	3
Functional MRI missing	2	0
Functional MRI quality	1(1)	3(4)

Neuroimaging acquisition and analysis

MRI acquisition. MRI data were acquired on a 3T Siemens Magnetom Verio (Siemens Healthcare, Erlangen, Germany) using a 32-channel head coil. We recorded task-free functional MRI using a T2*-weighted gradient 2D-EPI sequence (repetition time [TR]=2000ms, echo time [TE]=27ms, flip angle=90°; 37 slices tilted at approximately 30° with 3 mm slice thickness, field of view [FOV]=210×210mm2, matrix=70×70, 3×3×3 mm3 voxels, 1 mm gap; 210 volumes per session). We also acquired a T1-weighted 3D-MPRAGE sequence (176 sagittal slices, TR=2300 ms, TE=2.98 ms, inversion time [TI]=900 ms, flip angle=7°, FOV=240×256 mm^2, matrix=240×256, 1×1×1 mm^3 voxels). Throughout the duration of our longitudinal study, imaging hardware and console software (Syngo B17) were held constant. Participants also underwent multiple functional tasks, which had a variable number of volumes due to the different lengths of the tasks, but otherwise identical sequence parameters analogous to the task-free data (Kanske et al., 2015; Trautwein et al., 2016). During the functional session, participants were instructed to lie still in the scanner, think of nothing in particular, and fixate a white cross in the center of a black screen.

Task-free functional MRI analysis. Processing was based on DPARSF/REST for Matlab [http://www.restfmri.net (Song et al., 2011)]. We discarded the first 5 volumes to ensure steady-state magnetization, performed slice-time correction, motion correction and realignment, and co-registered functional time series of a given subject to the corresponding T1-weighted MRI. Images underwent unified segmentation and registration to MNI152, followed by nuisance covariate regression to remove effects of average WM and CSF signal, as well as 6 motion parameters (3 translations, 3 rotations). We included a scrubbing (Power et al., 2012) that modelled time points with a frame-wise displacement of ≥0.5 mm, together with the preceding and subsequent time points as separate regressors during nuisance covariate correction. Volume-based timeseries were mapped to the fsaverage5 surface using bbregister.

Gradient construction. In line with previous studies evaluating functional gradients (Bethlehem et al., 2020; Hong et al., 2019; Margulies et al., 2016; Paquola et al., 2019; Vos de Wael et al., 2020; Vos de Wael et al., 2018) the functional connectivity matrix was proportionally thresholded at 90% per row and converted into a normalised angle matrix using the BrainSpace toolbox for MATLAB (Vos de Wael et al., 2020). Diffusion map embedding, a nonlinear manifold learning technique (Coifman et al., 2005), identified principal gradient components, explaining functional connectivity variance in descending order. In brief, the algorithm estimates a low-dimensional embedding from a high-dimensional affinity matrix. In this space, cortical nodes that are strongly interconnected by either many suprathreshold edges or few very strong edges are closer together, whereas nodes with little or no functional connectivity are farther apart. The name of this approach, which belongs to the family of graph Laplacians, derives from the equivalence of the Euclidean distance between points in the embedded space and the diffusion distance between probability distributions centred at those points. It is controlled by the parameter α, which controls the influence of the density of sampling points on the manifold ($\alpha = 0$, maximal influence; $\alpha = 1$, no influence). Based on previous work (Margulies et al., 2016), we set $\alpha = 0.5$, a choice that retains the global relations between data points in the embedded space and has been suggested to be relatively robust to noise in the functional connectivity matrix. The diffusion time (t),

which controls the scale of eigenvalues of the diffusion operator was set at t=0 (default). Individual embedding solutions were aligned to the group-level embedding based on the Human Connectome Project S1200 sample (Van Essen et al., 2013) via Procrustes rotations (Vos de Wael et al., 2020). The Procrustes alignment enables comparison across individual embedding solutions, provided the original data is equivalent enough to produce comparable Euclidean spaces.

3D gradient metric: eccentricity. To construct the combined gradient, we computed the Euclidean distance to the individual center for gradient 1-3. Next, to evaluate change within and between individuals, we computed the difference between gradient scores between different time-points.

3D gradient metric: dispersion. To investigate multi-dimensional differences in cortical organization, we quantified dispersion of task-based networks (Kanske et al., 2015; Trautwein et al., 2016) and functional networks (Yeo et al., 2011) in 3D space. Each axis of this 3D space was defined by the values along the first three gradients. Within network dispersion was quantified as sum squared Euclidean distance of network nodes to the network centroid at individual level. Between network dispersion was calculated as the Euclidean distance between network centroids. These metrics were calculated for each subject within the individualized, aligned gradient space similar to previous work (Bethlehem et al., 2020).

Graph theoretical metrics. To further validate our gradient-based metric of integration and segregation, we also computed clustering coefficient and path length using the Brain Connectivity Toolbox (Rubinov and Sporns, 2010). Both measures were computed in the parcel-level, by averaging the individual connectomes within the 400 Schaefer parcels (Schaefer et al., 2018) and with a threshold at the top 10% of connections, analogue to our gradient approach.

Task-based functional networks. Paradigms identifying functional localizers are previously described (Kanske et al., 2015; Trautwein et al., 2016). In short, the attention network was defined based on the conjunction of activation following selective attention and executive control during a cued-flanker task. The socio-affective network was based on the contrast between emotional and non-emotional videos and the socio-cognitive network was based on the contrast between ToM and non-ToM questions. Networks were mapped to the fsaverage5 surface-template to evaluate their embedding within the intrinsic gradient space constructed from the resting-state fMRI data.

Behavioral markers

We assessed a battery of behavioral markers developed and adapted to target the main aims of the *Presence, Perspective,* and *Affect* modules: selective attention, compassion, and ToM. Behavioral changes of these markers elicited by the different modules are reported elsewhere (Trautwein et al., 2020). The measure for compassion was based on the EmpaToM task, a developed and validated naturalistic video paradigm in the current subjects (Kanske et al., 2015; Tholen et al., 2020). Videos showed people recounting autobiographical episodes that were either emotionally negative (e.g., loss of a loved one) or neutral (e.g., commuting to work), followed by Likert-scale ratings of experienced valence and compassion. Since the conceptual understanding of compassion might change due to the training, we ensured a

consistent understanding by defining it prior to each measurement as experiencing feelings of care, warmth, and benevolence. Compassion was quantified as mean of compassion ratings across all experimental conditions. The EmpaToM task (Kanske et al., 2015) also allowed for measurement of ToM performance. After the ratings, multiple-choice questions requiring inference of mental states (thoughts, intentions, beliefs) of the person in the video or factual reasoning on the video's content (control condition) were asked. Questions had three response options and only one correct answer, which had been validated during pre-study piloting (Kanske et al., 2015). Here, we calculated participants' error rates during the ToM questions after the video, collapsed across neutral and negative conditions.

Statistical analysis

Analysis was performed using SurfStat for Matlab (Worsley et al., 2009). We employed linear mixed-effects models, a flexible statistical technique that allows for inclusion of multiple measurements per subjects and irregular measurement intervals (Pinheiro and Bates, 2000). In all models, we controlled for age and sex, and random effect of subject. Inference was performed on subject-specific eccentricity/gradient change maps, Δeccentricity/gradient, which were generated by subtracting vertex-wise eccentricity/gradient maps of subsequent time points for a given participant.

a) Assessing module-specific change. To compare the modules against each other, we contrasted change of one given module against the average of the other two modules. To compare two modules, we compared one training module against another (for example *Affect* versus *Perspective*). To compare a given module against RCC, we estimated contrasts for training cohort change relative to RCC (*Presence, Perspective, Affect*).

b) Correction for multiple comparisons. Whole brain findings were corrected for multiple comparisons using random field theory for non-isotropic images (Worsley et al., 1999) with cluster-forming thresholds of p=0.005, two-tailed. Post-hoc network-based assessments were corrected for number of tests within the analysis step using FDR correction (Benjamini and Hochberg, 1995). Post-hoc whole cortex eccentricity/gradient change in TC1 and TC2 separately were thresholded with cluster-forming threshold at p=0.01, two-tailed.

c) Global signal regression. To assess the effects of global signal on our main longitudinal results we created connectivity matrixes while regressing out global signal within a 400 parcel solution (Schaefer et al., 2018) and captured change within task-based networks.

Theoretically, the cross-over design of the study and the inclusion of number of scans since baseline as covariance controlled for test-retest effects on motion (as participants may become calmer in scanner after repeated sessions). Nevertheless, to control for outliers, we removed all individuals with >0.3 mm/degree movement (Power et al., 2012).

Behavioral prediction

We adopted a supervised machine learning framework with cross-validation to predict behavioral change based on change in functional connectivity organization. We aimed at predicting attention, compassion, and perspective-taking (**Figure 4**). We regressed out age and sex, and computed a binned change score to account for outliers. We utilized 5-fold cross-validation separating training and test data. Feature selection procedure was conducted using the training data (4/5 segments) and it was repeated 5 times with different segments of

training data. Based on our vertex wise manifold summary, a set of features that could predict each behavioral score was identified using Lasso regularization, i.e. an L1 penalization on the parameters. Linear regression for predicting behavioral scores was constructed using the selected features as independent variables within the training data (4/5 segments) and it was applied to the test data (1/5 segment) to predict their behavioral scores. Prediction procedure was repeated 5000 times with different set of training and test data to avoid bias for separating subjects. The prediction accuracy was assessed by calculating Pearson's correlation between the actual and predicted behavioral scores as well as their mean absolute error, MAE (Chang et al., 2015).

Meta-analytical decoding

We used the NeuroSynth meta-analytic database (http://www.neurosynth.org) (Yarkoni et al., 2011) to assess topic terms associated with social, affective, interoceptive, and cognitive functioning. (*"affect", "autonomic", "emotion", "emotion regulation", "empathy", "episodic memory", "goal directed", "interoceptive", "mentalizing", "reward", "self", "semantic memory", "social", "social interaction", "theory mind", "inhibition", "executive", "cognitive control", "attention", "working memory"*). We used a t-test to compare there was significantly activation associated with a certain term relative to the activity outside the task-based activation. Following, after correcting for number of contrasts tested, we plotted the functions significantly associated with the respective task-based activation.

Transcriptomic association analysis

To provide additional neurobiological context of our findings, we assessed spatial correlations of task-based functional activations in attention and socio-affective, and socio-cognitive processing and gene expression patterns. Initially, we correlated the t-statistics map of the functional activations and the post-mortem gene expression maps provided by Allen Institute for Brain Sciences (AIBS) using the Neurovault gene decoding tool (Gorgolewski et al., 2014; Hawrylycz et al., 2012). Neurovault implements mixed-effect analysis to estimate associations between the input t-statistic map and the genes of AIBS donor brains yielding the gene symbols associated with the input t-statistic map. Gene symbols that passed a significance level of FDR-corrected $p < 0.05$ and showed a positive association with the task-based were further tested whether they are consistently expressed across the donors using abagen toolbox (https://github.com/rmarkello/abagen)(Arnatkeviciute et al., 2019). For each gene, we estimated whole-brain gene expression map and correlated it between all pair of different donors. Genes showing consistent whole-brain expression pattern across donors ($r>0.5$). In a second stage, gene lists that were significant were fed into enrichment analysis, which involved comparison against developmental expression profiles from the BrainSpan dataset (http://www.brainspan.org) using the cell-type specific expression analysis (CSEA) developmental expression tool (http://genetics.wustl.edu/jdlab/csea- tool-2) (Dougherty et al., 2010). As the AIBS repository is composed of adult post-mortem datasets, it should be noted that the associated gene symbols represent indirect associations with the input t-statistic map derived from the developmental data.

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CHANGING THE SOCIAL BRAIN: PLASTICITY ALONG MACRO-SCALE AXES OF FUNCTIONAL CONNECTIVITY FOLLOWING SOCIAL MENTAL TRAINING

SUPPLEMENT

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SUPPLEMENTARY MATERIALS AND METHODS

Training modules

Each module started off with a three-day intensive retreat, followed by weekly group sessions with the teachers and daily home practice supported by a custom-made internet platform and smartphone applications providing: i) audio streams for guided meditations and ii) an interface for dyadic exercises (**Figure 1**) (Singer et al., 2016). During the retreat, participants were introduced to topics and associated core exercises of the upcoming module. Training during the subsequent eight weeks included weekly two-hour-long sessions with instructors that included discussion of training challenges and effects, practice of the core exercises, and introduction to new contemplative practices. The last five weeks of each module were used to consolidate previous topics, with no new topics being introduced. Presence modules were always first in order to stabilize the mind and prepare the participants for the socio-cognitive and socio-affective training modules.

Presence: Core exercises, practiced repeatedly during the retreat, in the weekly sessions, and at home (instruction was to practice at least five times per week), were Breathing Meditation and Body Scan (Kabat-Zinn, 1990). The instruction for the Breathing Meditation was to focus attention on sensations of breathing and to refocus attention whenever it drifted. The Body Scan involved focusing on various parts of the body in a systematic fashion (*e.g.*, from toes to head), while paying close attention to perceptions occurring in these body parts. Additional exercises of Presence, also practiced during the retreat and weekly sessions, were walking meditation, meditations on vision, sound, and taste, as well as an open presence meditation. These practices require a deliberate focus of attention on certain facets of present moment-to-moment experience, monitoring of distractions, and reorienting towards the object of attention in the meditation, be it the breath, a sound or a visual object.

Affect: Core exercises were Loving-kindness Meditation (Salzberg, 1995) and the 'Affect Dyad' (Kok and Singer, 2016; Singer et al., 2016). For Loving-kindness Meditation, participants were first familiarised to ways of connecting with the feeling and motivation of love and care, such as imagining a baby, a cute animal, a close benevolent other, a place of safety and comfort, or focusing on sensations of warmth in the body. These feelings can then be directed towards oneself and others. The typical instruction for the Loving-kindness Meditation was to start with imagining oneself and then a benefactor, where such feelings might arise naturally, and then to extend feelings of Loving-kindness and good wishes to self and then the benefactor. Over the course of several sessions, participants were asked to successively extent these feelings to others to whom one feels neutral, people one has difficulties with, and ultimately all humans and sentient beings. To foster experiences of Loving-kindness, participants were instructed to mentally repeat phrases such as "May you be happy", "May you be healthy", "May you be safe", and "May you live with ease".

The Affect Dyad is a partner practise done face-to-face during the retreat, during the weekly sessions, and via the web- or smartphone-based application during daily practice at home. During this exercise, participants contemplated situations from their last day that they experienced as difficult and situations which they were grateful for. Partner A was instructed to listen attentively to what the speaker (partner B) has to say without giving verbal or non-

verbal feedback, promoting empathic listening. The speaker remembered the situation and how it felt like and focused on the immediate subjective affective and bodily experience without engaging in abstract reasoning or interpretation. After a first run, roles were switched. This contemplative dialogue allows cultivating empathic listening in the listener and observing difficult emotions and their effect on the body as well as developing gratitude and positive affect in the speaker. Additional features of *Affect* were exploration of emotions in an attitude of acceptance and care, a guided mental training that contrasts empathy and compassion and teaches participants how to transform an empathic into a loving and compassionate response when confronted with the suffering of others (Klimecki et al., 2014), forgiveness meditation, and development of self-compassion (Neff and Germer, 2013).

Perspective: Core exercises were an Observing-thoughts Meditation and a 'Perspective Dyad'. In the former, the objective was to observe thoughts as mental events or natural phenomena and not as direct representations of reality. In the starting phase of the practice, this was supported by identifying thoughts using opposite poles such as me/other, past/future, positive/negative, or more generic labels such as "judging" and "thinking". Later in the program, participants were instructed to observe the coming and going of thoughts without getting involved in them.

The Perspective Dyad is a partner exercise with a structure comparable to the Affect Dyad. This exercise was partly based on the Internal Family System approach by Schwartz and colleagues (Holmes, 2007; Schwarz, 1997) and on theoretical accounts distinguishing between affective (*e.g.*, compassion and empathy) and cognitive (*e.g.*, Theory of Mind, ToM) routes of social cognition (Singer, 2006, 2012). For this training of perspective-taking on self and others, participants were first introduced to the concept of inner parts, personality-trait-like patterns of cognition, emotion, and behavioral tendencies that dominate in certain situations and shape experience as well as behavior (Holmes, 2007). During the retreat and throughout the course, participants were supported in detecting inner parts. In the Perspective Dyad, the speaker described a situation of the last day from the perspective of one of his/her inner parts, that is, how the experience might have been if a certain inner part had been dominant. The other participant listened attentively without giving verbal or non-verbal feedback and tried to find out from which inner part the speaker was recounting the situation. The listener, thus, had to engage in cognitive perspective-taking on the other to find out "who is speaking" and to infer the needs, desires, and beliefs of the other. The speaker, in turn, needed to take a meta-perspective onto its own self-related aspects and to decouple from a lived and experienced reality. Additional elements of *Perspective* were exercises in which participants needed to take the perspective of people they encountered whom they have difficulties with in their daily lives, reflections on the central role that thoughts play in our lives, how these might differ for thoughts of others, and why understanding them differs from approving their behavior. This description of the training protocol was adapted from previous work (Singer et al., 2016; Valk et al., 2017).

SUPPLEMENTARY RESULTS

Task-based activation patterns in attention, socio-affect, and socio-cognitive function.

Assessing task-based activation patterns in attention, socio-affect, and socio-cognition. (**Figure 1**), we observed task-specific and task-general activations between attention and social functioning. Attention processing (*i.e.,* the overlap between stimulus driven reorienting and executive control in the cued-flanker task) was associated with functional activations in bilateral inferior parietal and superior frontal regions. On the other hand, socio-affective processing (*i.e.,* the contrast of viewing emotional and neutral videos in the EmpaTom task), implicated bilateral supramarginal, dorsolateral prefrontal and bilateral inferior frontal regions. ToM (*i.e.,* the contrast of ToM versus no-ToM questions in the EmpaToM) related to activations in bilateral temporal and temporo-parietal, as well as medial prefrontal regions. Attention and socio-affective processing both implicated the bilateral anterior insula and anterior midline regions, and socio-affective and socio-cognitive processing both related to temporal parietal, midline parietal and prefrontal, as well as inferior frontal regions, although the peaks of the activation pattern in these broader brain areas clearly differ for the socio-affective and socio-cognitive domains (see also (Kanske et al., 2015)). Our findings are thus in line with previous work and demonstrate differentiable, but overlapping networks for attention, socio-emotional, and socio-cognitive activations (Schurz et al., 2020a).

Leveraging eccentricity against graph theoretical measures

To further validate our gradient-based model of eccentricity (segregation and integration) we also created metrics of regional integration and segregation using graph theoretical approaches (**Figure S1**). We found a positive correspondence between gradient-based eccentricity and graph theory-based clustering coefficient ($r=0.641$, $p<0.001$) and path length ($r=0.510$, $p<0.001$). Evaluating network-specific alterations following mental training these measures, we found increases of clustering coefficient (attention network: $t=2.489$, $p=0.021$) and path length (socio-cognitive network: $t=2.374$, $p=0.027$) following *Presence* training and decreases in both measures (clustering coefficient: socio-cognitive network: $t=-2.629$, $p=0.015$ and path length attention network: $t=-2.43$, $p=0.03$, socio-affective network: $t=-2.843$, $p=0.01$, socio-cognitive network: $t=-3.335$, $p=0.003$).

Eccentricity change in each training cohort

Evaluating the alterations in each training cohort separately we observed similar effects (**Figure S2**). Specifically, in TC1 we found increases in eccentricity of left TPJ following *Presence* and decreases following *Perspective* (FWEp<0.05). In addition, we found decreases following *Perspective* in right superior temporal and right temporal pole (FWEp<0.05). Studying the changes in task-based networks, we observed increases in eccentricity following *Presence* in socio-affective ($t=2.54$, $p=0.03$) and socio-cognitive ($t=3.14$, $p=0.005$) networks and decreases in eccentricity following *Perspective* in the socio-cognitive task-based network ($t=-3.07$, $p=0.006$). For TC2, we found increases in eccentricity in right opercular and right inferior temporal/ occipital regions following *Presence* and decreases in right inferior temporal/occipital regions following *Perspective* (FWEp<0.05).

Evaluating change against retest controls, we observed a decrease of eccentricity following *Perspective* in task-based socio-cognitive network (t=-2.10, p=0.05) at uncorrected thresholds. Last, evaluating change between two modules, we observed difference between *Presence* and *Perspective* in task-based attention networks (t=2.54, p=0.04) and socio-cognitive networks (t=3.22, p=0.005).

Global signal corrected analyses

Correcting the functional connectivity matrices for global signal (GSR) before computing gradient and eccentricity measures gave similar results as without GSR (**Figure S3**). Specifically, along G1 we found a difference between attention and socio-affect network (t=-5.228, p<0.001) and between the attention and socio-cognitive network (t=-5.63, p<0.001). Along G2 we observed a difference between socio-affect and socio-cognitive network (t=-2.813, p=0.015). Along G3 we observed a difference between all networks; attention versus socio-affect (t=-6.353, p<0.001), attention versus socio-cognition (t=-9.283, p<0.001), and socio-affect and socio-cognition (t=-2.96, p=0.01). Testing alterations following training, we observed that eccentricity increases in attention task-based networks following *Presence* (t=2.232, p=0.04), and decreased in attention task-based network (t=-2.50, p=0.015) following *Perspective*. In individual gradients we found that, along G1, the attention network decreased following *Presence* (t=-2.157, p=0.048). For G2, *Presence* resulted in a decrease of the socio-cognitive network (t=-2.918, p=0.006).

Social connections with eccentricity of functional communities.

Evaluating longitudinal change within large-scale functional communities (Yeo et al., 2011) (**Figure S4**), we found that *Presence* training resulted in increased eccentricity of dorsal attention networks (t=3.67, p=0.002) and ventral attention networks (t=2.81, p=0.04). Conversely, *Perspective* training resulted in decreased embedding of dorsal attention networks (t=-3.13, p=0.02) and ventral attention network (t=-2.76, p=0.05). Studying change in the individual large-scale gradients (G1-G3), we observed increases in the ventral attention network following *Affect* (t=3.00, p=0.02) along G1. Last we observed decrease of the visual network following *Affect* (t=-4.02, p<0.001) along G3.

Change in first three large-scale gradients in each training cohort

Reiterating analysis of **Figure 2** in each training cohort separately (**Figure S5** and **Figure S6**), we observed decreases in G1 following *Presence* in right superior parietal cortex extending to supramarginal gyrus in TC1 (FWEp<0.05). Conversely, *Affect* resulted in increases in G1 in right superior parietal cortex extending to supramarginal gyrus in TC1. In TC2, we observed increases in bilateral mid/anterior insula following *Affect* (FWEp<0.05). In task-based networks, we found the socio-cognitive network showed increases following *Perspective* in TC1 (t=2.62, p<0.03). Along G2, we observed whole cortex alterations in TC2 for *Presence*, with increases in right lateral frontal regions and decreases of socio-affect task-based network (t=-2.86, p=0.02) following *Affect* in this cohort. Along G3 we found decreases in left superior frontal regions following *Perspective* in TC2 (FWEp<0.05).

Evaluating changes along G1-G3 in different contrasts, we observed no change relative to retest controls, but decreases in *Affect* relative to *Presence* in socio-cognitive networks (t=-2.05, p=0.05) along G1 at uncorrected threshold. For G2 we also observed no change relative to retest controls but increases in *Presence* relative to *Perspective* in socio-affective networks (t=1.98, p=0.05, uncorrected), Affect relative to Presence in attention networks (t=-2.20, p=0.03, uncorrected) and socio-affective networks (t=-2.37, p=0.02 uncorrected). For G3 we observed no change versus RCC or between groups.

Behavior change prediction

Attention was not predictable using a multi-gradient approach (raw: r=-0.21, p=0.06; bin: r=-0.04, p>0.1). Compassion and perspective-taking were less predictable using raw scores (compassion raw: r=0.19, p=0.06, MAE=0.504; perspective-taking raw: r=0.20, p=0.05, MAE=0.099), yet distribution of weight maps was similar (**Figure S7**).

Functional decoding of localizer networks

Decoding task-based activations using large-scale functional communities (Yeo et al., 2011) we found that task-based activations associated with attention were predominantly in dorsal and ventral attention networks and fronto-parietal networks (**Figure S4**). Conversely, task-based activations associated with socio-affective processing related to frontal parietal networks as well as default mode network and ventral attention network. ToM-based activations were associated with default mode network, and ventral attention and somato-sensory network.

To further decode the association between task-based activations of social processing in the current sample we took an ad-hoc a meta-analytic approach using meta-analytic maps of social, cognitive, affective, and attentional terms in the Neurosynth database (**Figure S8**). We found differential relationships between each of the functional localizers and meta-analytical maps (FDRq<0.05). Task-based activation of attention was associated with inhibition, executive functioning, cognitive control, attention, and working memory. Conversely, task-based activation of socio-affective functioning was associated with affect, goal-directed behavior, episodic memory, executive functioning, emotion, social-interaction, cognitive control, emotion regulation, inhibition, self, empathy, social, ToM, and mentalizing. Socio-cognitive task-based activations related to episodic memory, semantic memory, emotion, emotion regulation, empathy, social interaction, self, mentalizing, social, and ToM – meta-analytical maps.

Genetic decoding of the social brain

Having functionally decoded task-based activations associated with attention and social processing, we sought further understand the factors that contribute to the dissociable activation patterns of social functioning (**Figure S9, Tables S1-3**)

Specifically, we correlated the task-based activation during attention, socio-affective and socio-cognitive tasks with post-mortem gene expression data from the Allen Institute of Brain

Sciences (AIBS) (Hawrylycz et al., 2012). Among significantly associated genes, we selected only those consistently expressed (r>0.5) among donors. We then used developmental gene set enrichment analysis (Dougherty et al., 2010), to identify spatiotemporal time windows in which these genes are most frequently expressed. The analysis suggested a differential patterning between attention, socio-affective, and socio-cognitive processes. Activations associated with reorienting and executive control of attention were predominantly in cerebellum and thalamus during childhood and adolescence, and showed a positive increase along development (r=0.797, p=0.006), whereas socio-cognitive activations were associated with striatal expression in adolescence and early adulthood, and did not show association with development (r=-0.497, p>0.1). Socio-affective activations were associated with both thalamus in early fetal and adolescent time windows, as well as cerebellum across development, and had a negative relationship with developmental expression (r=-0.86, p=0.002).

Network-based metrics of eccentricity change

In addition, we computed network-level index of segregation and integration; the *dispersion* within as well as *distance* between task-based fMRI activations in 3D gradient space (Bethlehem et al., 2020) (**Supplementary Figure 10**). Using these metrics to evaluate change we found increased between network distance between attention and socio-affective (t=2.81, p=0.03) and attention and socio-cognitive (t=2.46, p=0.05) networks following *Presence.* Conversely, *Perspective* resulted in a decrease in between network distance between attention and socio-affective network (t=-2.42, p=0.05).

SUPPLEMENTARY FIGURES

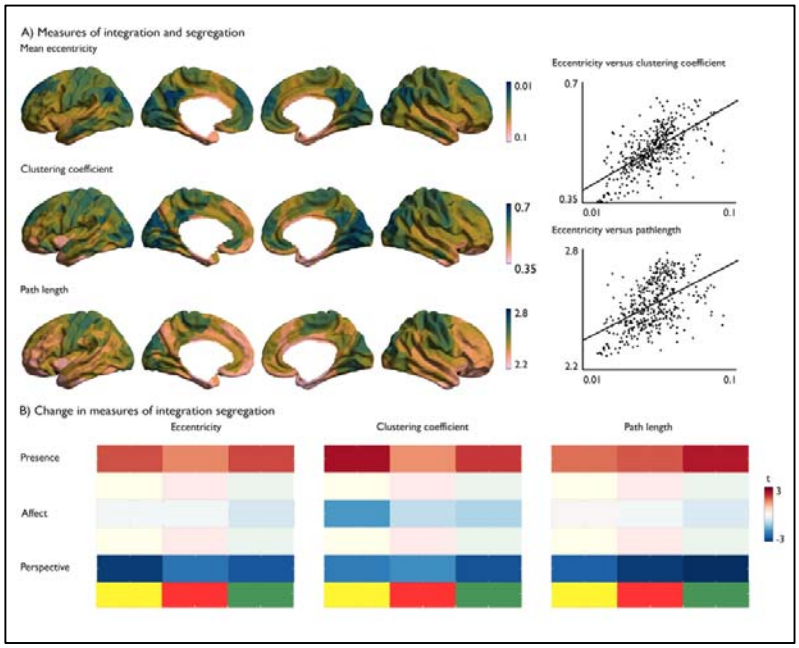

Figure S1. Comparison of gradient-based eccentricity measure with graph theory-based measures of integration and segregation. A) Measures of integration and segregation; B) Change in difference measures of integration and segregation (clustering coefficient and path length). Colors reflect the relevant task-based network (yellow is attention, red is socio-affect and green is socio-cognition).

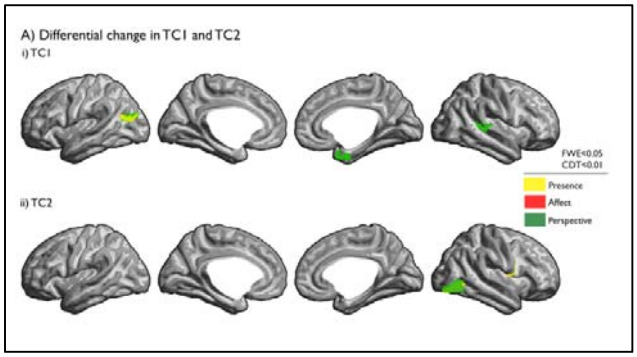

Figure S2. Module specific change in eccentricity in TC1 and TC2 separately. Whole brain differential change of manifold embedding in training cohort 1 (TC1) (i) and training cohort 2 (TC2) (ii), FWEp<0.01 two-tailed following each training versus the other two trainings

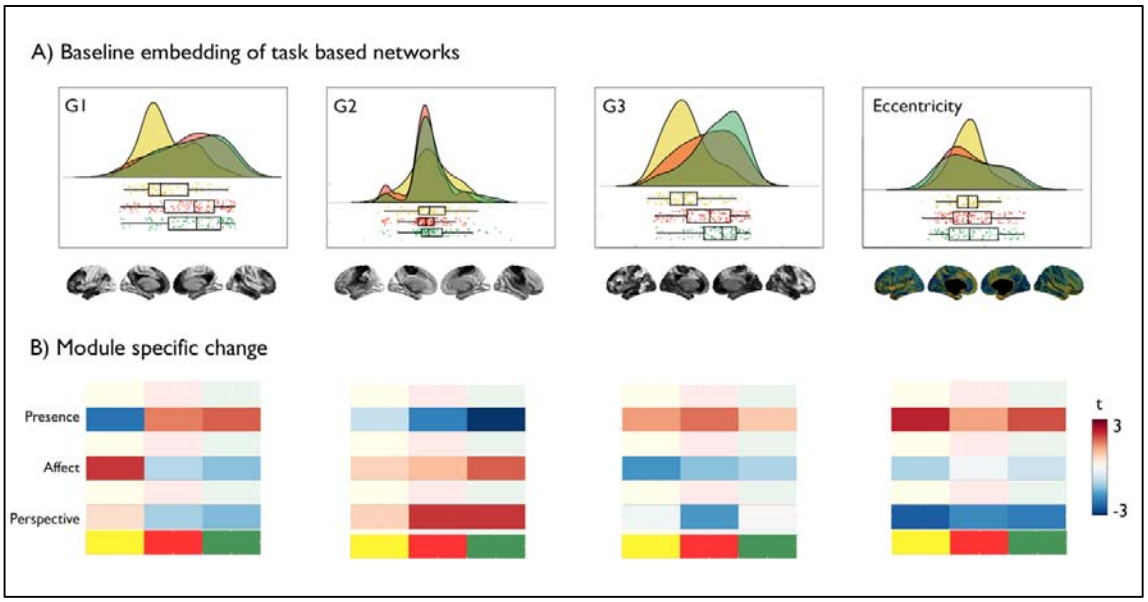

Figure S3. Large-scale organization of social brain and plasticity following training when controlling for GSR. Colors reflect the task-based networks.

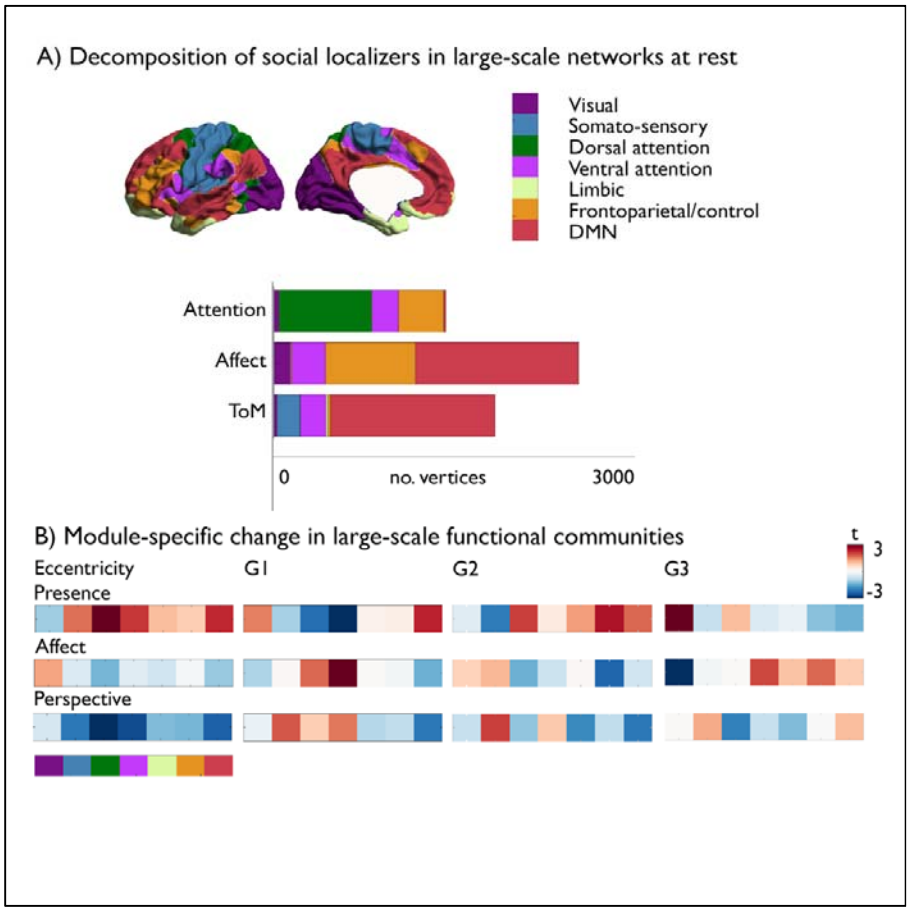

Figure S4. Functional community decoding. A) Decomposition of task-based functional activations into large-scale functional community's at rest (Yeo et al., 2011); **B**) Association between the change in embedding, and the first three gradients, of large-scale functional communities (Yeo et al., 2011) following mental training.

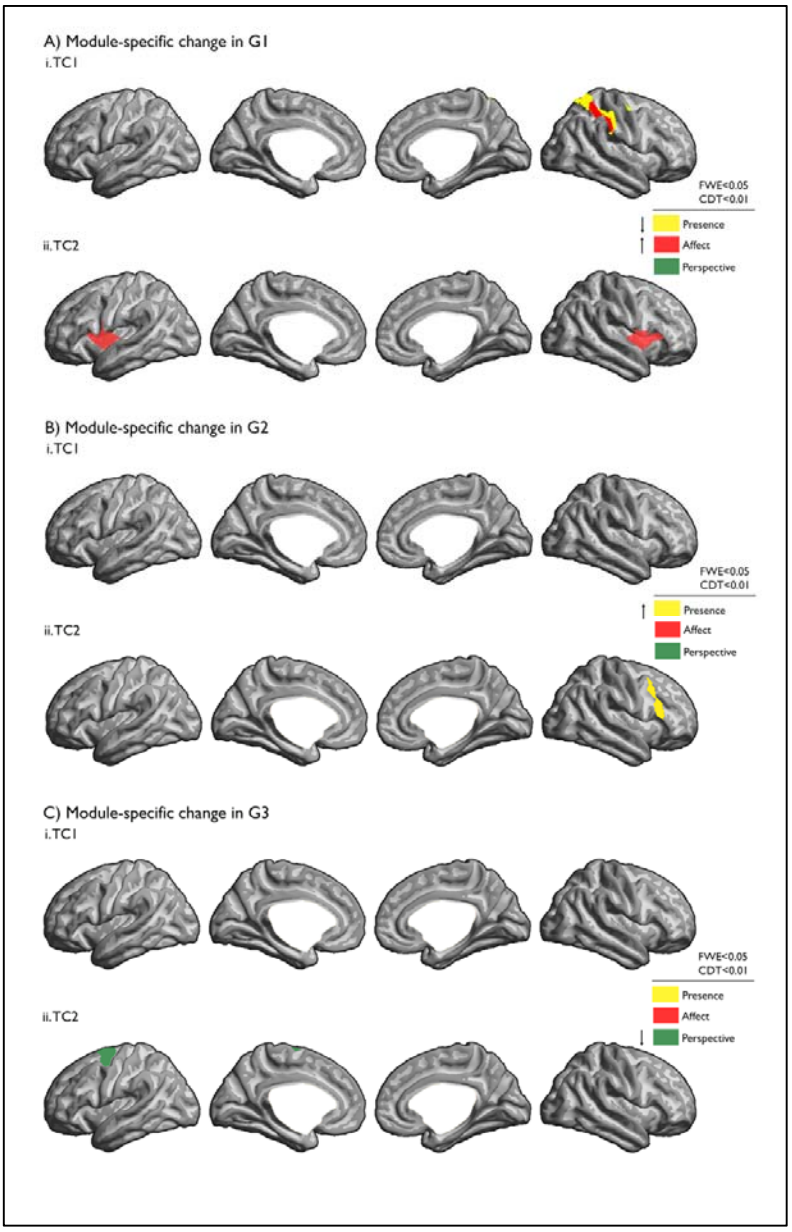

Figure S5. Gradient changes in TC1 and TC2 separately. Change in G1-G3 in training cohort 1 and 2, evaluated using a cortex-wide analysis, as well as within task-based networks.

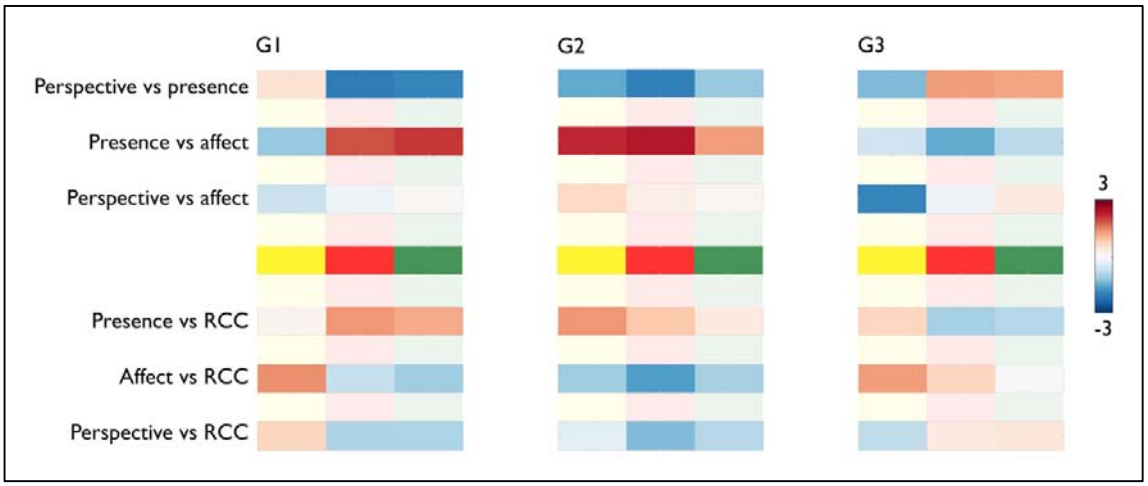

Figure S6. Change in G1-G3 vs other module and retest controls. Colors (yellow, red, green) reflect task-based network (attention, socio-affect and socio-cognition respectively), whereas red-blue ([-3 3]) indicates the t-value associated with change in each task-based network.

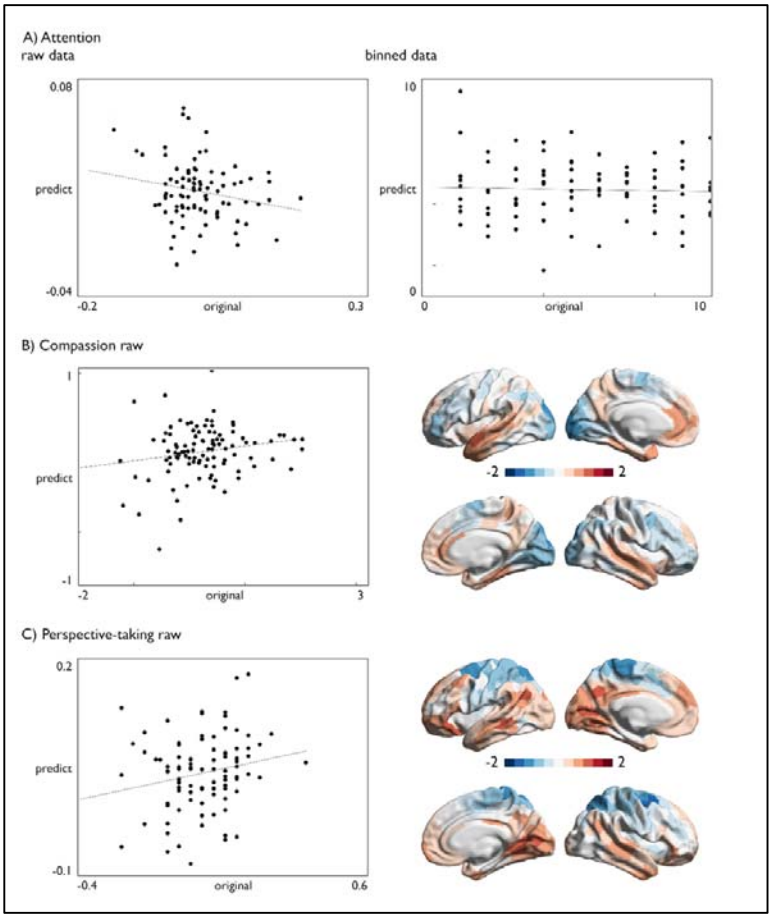

Figure S7. Predicting attention, compassion and ToM. A) Prediction of attention using raw and binned scores; **B**) Prediction of compassion and perspective-taking using raw change scores, as well as the associated weight maps (z-scored weights between -2 2 are visualized).

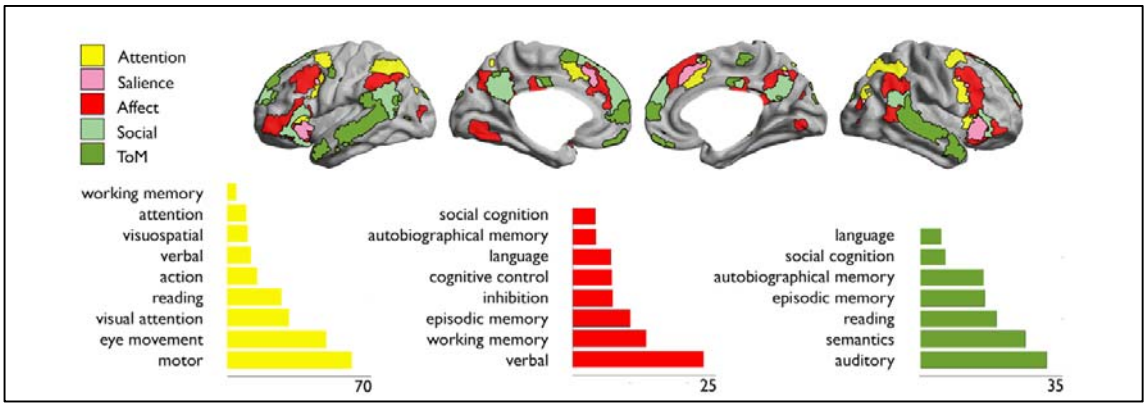

Figure S8. Functional decoding of task-based activations associated with attention, using 20 meta-analytical topic terms of Neurosynth reflecting social, affective, cognitive, and attentional functioning. Significant associations and associated t-values are represented in the bar plot, where yellow is attention, red is socio-affective, and green is socio-cognitive task-based activation maps.

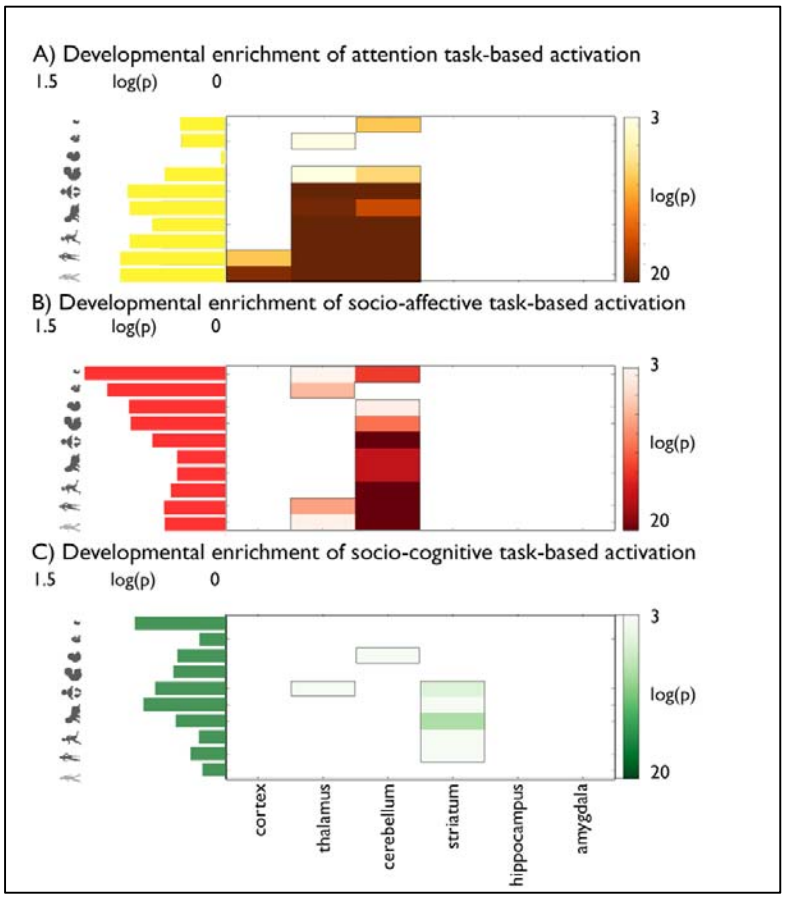

Figure S9. Developmental enrichment for each of the functional activations in attention, socio-affective, and socio-cognitive tasks at FDRp<0.05. The bar plot on the represents the log transformed p-values that averaged across all brain structures that reported in the enrichment analysis.

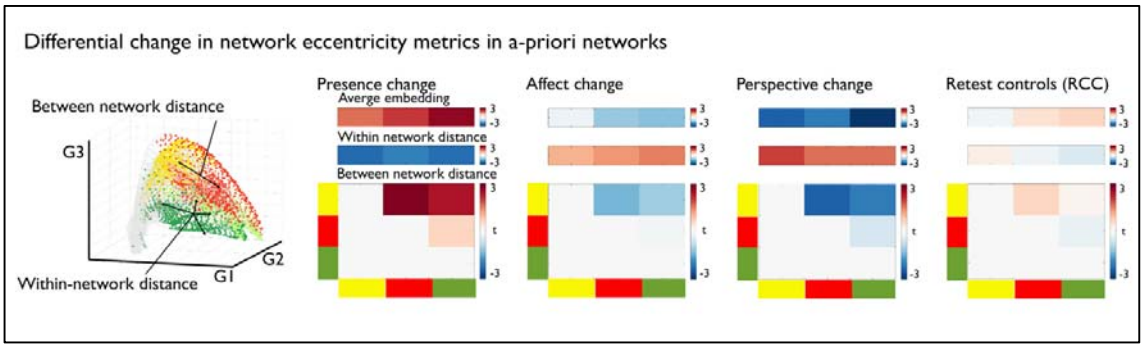

Figure S10. Differential change in eccentricity using network-based approaches. Average embedding recapitulates the average change score, within-network distance describes the change within each task-based network (yellow=attention, red=socio-affect, green=socio-cognition), between-network distance describes the change between task-based network. Effects are displayed as colored t-values [-3 3].

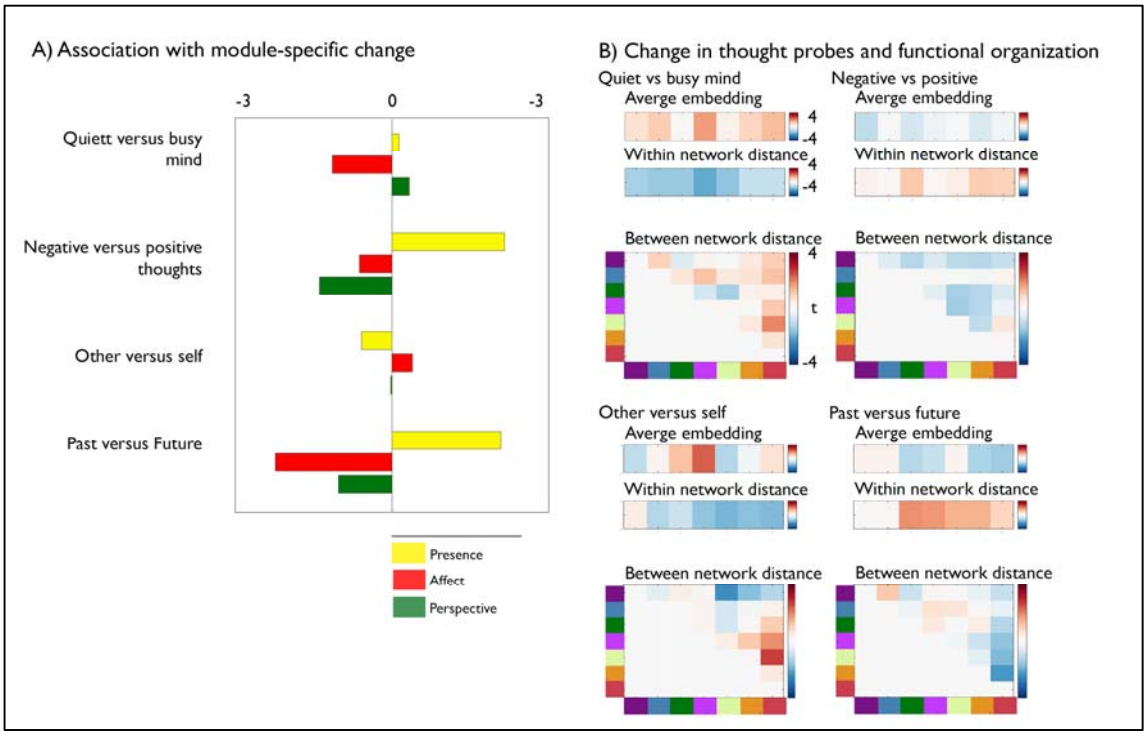

Figure S11 Association between change in task-unrelated thoughts and functional embedding. Change in task-related thought probes per module, and association with functional organization.

1 **SUPPLEMENTARY TABLES**

ACAN	DCUN1D2	GPX3	MAP3K13	PVALB	SULF1
ACYP2	DENND2D	GSTT1	MAP9	QRFPR	SV2C
ADM	DEXI	GUCA2B	MCF2	RAB37	SYCP2
ALDH1A3	DNAJC4	HAPLN4	MFGE8	RAD54B	SYT2
AMDHD1	DSCC1	HR	MGST2	RAMP3	TFAM
ANK1	ECSIT	HS3ST1	MIR31HG	RCAN2	THAP10
ANKRD34C	EFNA5	HS3ST5	MREG	RELL2	TIFA
AR	EIF5A2	IGDCC3	MX1	RET	TPTE2P6
ARHGAP9	ELMO3	INA	MYH7B	RFPL1	TRAK2
ASB13	EPB41	INTS8	NEFH	RHOBTB2	TRPC3
ATG4D	EPN3	IPW	NR1D2	RILP	TTC39A
AVPI1	ERRFI1	IRS1	NR3C1	RORA	TTC39B
BCAT1	ESRRG	ISCU	NRIP2	RPP25	UPP1
BTBD17	EXTL2	KCNA2	NT5M	RSRC1	VAV3
C17orf75	FAM20A	KCNAB3	NXPH3	SAP30L	
C3orf18	FAM71E1	KCNC1	ONECUT1	SCN1A	
C6orf106	FBLN7	KCNC3	ONECUT2	SCN1B	
CACNA2D2	FBXO9	KCTD9	OPRM1	SCRT1	
CAMK2D	FER1L4	KNG1	P2RX6	SDSL	
CAMK2G	FES	KRT31	PAG1	SEMA7A	
CCNI	FGF18	LAG3	PCDH12	SHD	
CDH7	FGF9	LAMA2	PCP4	SIX4	
CDR2L	FLT3	LAPTM4B	PGK1	SLC16A6	
CDS1	FNDC5	LCP2	PHLDA2	SLC17A6	
CERK	FRAT1	LGALS1	PHYH	SLC25A5	
CITED2	FSTL1	LINC00473	PLCB4	SLC38A1	
CLEC2L	FSTL5	LINC00515	PLCH1	SLC39A13	
CMYA5	GAL	LRCH1	PLEKHH3	SLC39A14	
CNTN6	GDPD1	LRRC38	PLXDC1	SMPX	
CPNE9	GLS2	LRRC3B	PNKD	SPAG4	
CRTAC1	GPLD1	LUZP1	PPARGC1A	SPTSSB	
CTXN3	GPR137C	LYPLA1	PPTC7	ST8SIA1	
CUX1	GPR161	MADCAM1	PSMD12	STARD10	

DCBLD2	GPR68	MAGI3	PTCHD1	STARD5	

Table S1. Genes associated with attention network activations.

ALDH1A3	CITED2	FSTL5	IPW	PAG1	SCN9A
AMDHD1	CNTN6	FZD1	KCTD12	PGAP1	SLC38A1
ANK1	DCUN1D2	GPLD1	KLK10	PLCB4	SPON2
ANKRD34C	DENND2D	GPR137C	LRCH1	PLEKHH3	ST8SIA1
ANKRD6	EPB41	GPR68	N4BP2	PLSCR4	TGFBI
CACNA2D2	FABP7	GPX3	NANOS1	PLXNC1	TMEM159
CADM1	FLT3	HIST1H1D	NGB	RAVER2	UPP1
CAMK2D	FNDC5	IGDCC3	ONECUT1	RORA	WTIP
CDH7	FRAT1	INTS8	OPRM1	SCGN	

Table S2. Genes associated with compassion network activations

BSPRY	FER1L4	LRRC49	ONECUT2	SV2C
BTBD17	HS3ST5	LRRN1	PCP4L1	TRPC3
COCH	IPW	MGST2	RBMS1	VAV3
EIF2A	ITM2A	MRPL33	S100A13	WDR6
FABP6	KLHL13	NCOA3	SLC39A13	ZNF268
FANCI	LCA5	NEB	SRGAP1	

Table S3. Genes associated with perspective-taking functional activations

SUPPLEMENTARY REFERENCES

Alcala-Lopez, D., Smallwood, J., Jefferies, E., Van Overwalle, F., Vogeley, K., Mars, R.B., Turetsky, B.I., Laird, A.R., Fox, P.T., Eickhoff, S.B., and Bzdok, D. (2018). Computing the Social Brain Connectome Across Systems and States. Cereb Cortex 28, 2207-2232.

Alcala-Lopez, D., Vogeley, K., Binkofski, F., and Bzdok, D. (2019). Building blocks of social cognition: Mirror, mentalize, share? Cortex 118, 4-18.

Alves, P.N., Foulon, C., Karolis, V., Bzdok, D., Margulies, D.S., Volle, E., and Thiebaut de Schotten, M. (2019). An improved neuroanatomical model of the default-mode network reconciles previous neuroimaging and neuropathological findings. Commun Biol 2, 370.

Arnatkeviciute, A., Fulcher, B.D., and Fornito, A. (2019). A practical guide to linking brain-wide gene expression and neuroimaging data. Neuroimage 189, 353-367.

Assem, M., Glasser, M.F., Van Essen, D.C., and Duncan, J. (2020). A Domain-General Cognitive Core Defined in Multimodally Parcellated Human Cortex. Cereb Cortex 30, 4361-4380.

Barrett, L.F. (2017). The theory of constructed emotion: an active inference account of interoception and categorization. Soc Cogn Affect Neurosci 12, 1-23.

Barrett, L.F., and Satpute, A.B. (2013). Large-scale brain networks in affective and social neuroscience: towards an integrative functional architecture of the brain. Current opinion in neurobiology 23, 361-372.

Batson, C.D. (2009). These things called empathy. In The Social Neuroscience of Empathy, J. Decety, and W. Ickes, eds. (Cambridge, MA: MIT press), pp. 16-31.

Benjamini, Y., and Hochberg, Y. (1995). Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. Journal of the Royal Statistical Society Series B (Methodological) 57, 289-300.

Bertolero, M.A., Yeo, B.T., and D'Esposito, M. (2015). The modular and integrative functional architecture of the human brain. Proc Natl Acad Sci U S A 112, E6798-6807.

Bertolero, M.A., Yeo, B.T.T., and D'Esposito, M. (2017). The diverse club. Nat Commun 8, 1277.

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

Betzel, R.F., Fukushima, M., He, Y., Zuo, X.N., and Sporns, O. (2016). Dynamic fluctuations coincide with periods of high and low modularity in resting-state functional brain networks. Neuroimage 127, 287-297.

Buckner, R.L., Andrews-Hanna, J.R., and Schacter, D.L. (2008). The brain's default network: anatomy, function, and relevance to disease. Ann N Y Acad Sci 1124, 1-38.

Bzdok, D., Schilbach, L., Vogeley, K., Schneider, K., Laird, A.R., Langner, R., and Eickhoff, S.B. (2012). Parsing the neural correlates of moral cognition: ALE meta-analysis on morality, theory of mind, and empathy. Brain Struct Funct 217, 783-796.

Chanes, L., and Barrett, L.F. (2016). Redefining the Role of Limbic Areas in Cortical Processing. Trends Cogn Sci 20, 96-106.

Chang, L.J., Gianaros, P.J., Manuck, S.B., Krishnan, A., and Wager, T.D. (2015). A Sensitive and Specific Neural Signature for Picture-Induced Negative Affect. PLoS Biol 13, e1002180.

Chun, M.M., Golomb, J.D., and Turk-Browne, N.B. (2011). A taxonomy of external and internal attention. Annu Rev Psychol 62, 73-101.

Coifman, R.R., Lafon, S., Lee, A.B., Maggioni, M., Nadler, B., Warner, F., and 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, 7426-7431.

Corbetta, M., Patel, G., and Shulman, G.L. (2008). The reorienting system of the human brain: from environment to theory of mind. Neuron 58, 306-324.

Corbetta, M., and Shulman, G.L. (2002). Control of goal-directed and stimulus-driven attention in the brain. Nat Rev Neurosci 3, 201-215.
Cotier, F.A., Zhang, R., and Lee, T.M.C. (2017). A longitudinal study of the effect of short-term meditation training on functional network organization of the aging brain. Sci Rep 7, 598.
Craig, A.D. (2009). How do you feel--now? The anterior insula and human awareness. Nat Rev Neurosci 10, 59-70.
Dajani, D.R., and Uddin, L.Q. (2015). Demystifying cognitive flexibility: Implications for clinical and developmental neuroscience. Trends Neurosci 38, 571-578.
Dale, A.M., Fischl, B., and Sereno, M.I. (1999). Cortical surface-based analysis. I. Segmentation and surface reconstruction. Neuroimage 9, 179-194.
de Vignemont, F., and Singer, T. (2006). The empathic brain: how, when and why? Trends Cogn Sci 10, 435-441.
de Waal, F.B. (2012). The antiquity of empathy. Science 336, 874-876.
Dehaene, S., Kerszberg, M., and Changeux, J.P. (1998). A neuronal model of a global workspace in effortful cognitive tasks. Proc Natl Acad Sci U S A 95, 14529-14534.
Dougherty, J.D., Schmidt, E.F., Nakajima, M., and Heintz, N. (2010). Analytical approaches to RNA profiling data for the identification of genes enriched in specific cells. Nucleic Acids Res 38, 4218-4230.
Dunbar, R.I.M. (1998). The Social Brain hypothesis. Evol Anthropol 6, 178-190.
Duncan, J. (2010). The multiple-demand (MD) system of the primate brain: mental programs for intelligent behaviour. Trends Cogn Sci 14, 172-179.
Eisenberg, N., and Fabes, R.A. (1990). Empathy: conceptualization, measurement, and relation to prosocial behavior. . Motivation and Emotion 14, 131-149.
Finc, K., Bonna, K., He, X., Lydon-Staley, D.M., Kuhn, S., Duch, W., and Bassett, D.S. (2020). Dynamic reconfiguration of functional brain networks during working memory training. Nat Commun 11, 2435.
First, M.B., Gibbon, M., Spitzer, R.L., Williams, J.B.W., and Benjamin, L.S. (1997). Structured Clinical Interview for DSM-IV Axis II Personality Disorders, (SCID-II). (Washington, D.C.: American psychiatric Press, Inc.).
Frith, C.D., and Frith, U. (2006). The neural basis of mentalizing. Neuron 50, 531-534.
Frith, U., and Frith, C.D. (2003). Development and neurophysiology of mentalizing. Philos Trans R Soc Lond B Biol Sci 358, 459-473.
Gorgolewski, K.J., Fox, A.S., Chang, L.J., Schaefer, A., Arelin, K., Burmann, I., Sacher, J., and Margulies, D.S. (2014). Tight fitting genes: finding relations between statistical maps and gene expression patterns. In OHBM 2014.
Gratton, C., Laumann, T.O., Nielsen, A.N., Greene, D.J., Gordon, E.M., Gilmore, A.W., Nelson, S.M., Coalson, R.S., Snyder, A.Z., Schlaggar, B.L., *et al.* (2018). Functional Brain Networks Are Dominated by Stable Group and Individual Factors, Not Cognitive or Daily Variation. Neuron 98, 439-452 e435.
Haak, K.V., and Beckmann, C.F. (2020). Understanding brain organisation in the face of functional heterogeneity and functional multiplicity. Neuroimage 220, 117061.
Haak, K.V., Marquand, A.F., and Beckmann, C.F. (2018). Connectopic mapping with resting-state fMRI. Neuroimage 170, 83-94.
Hansen, J.Y., Markello, R.D., Vogel, J.W., Seidlitz, J., Bzdok, D., and Misic, B. (2021). Mapping gene transcription and neurocognition across human neocortex. Nat Hum Behav.
Hawrylycz, M.J., Lein, E.S., Guillozet-Bongaarts, A.L., Shen, E.H., Ng, L., Miller, J.A., van de Lagemaat, L.N., Smith, K.A., Ebbert, A., Riley, Z.L., *et al.* (2012). An anatomically comprehensive atlas of the adult human brain transcriptome. Nature 489, 391-399.
Holmes, T. (2007). Parts word: An illustrated guide to your inner life (Kalamazoo: Winged Heart Press).

Hong, S.J., Vos de Wael, R., Bethlehem, R.A.I., Lariviere, S., Paquola, C., Valk, S.L., Milham, M.P., Di Martino, A., Margulies, D.S., Smallwood, J., and Bernhardt, B.C. (2019). Atypical functional connectome hierarchy in autism. Nat Commun 10, 1022.

Hong, S.J., Xu, T., Nikolaidis, A., Smallwood, J., Margulies, D.S., Bernhardt, B.C., Vogelstein, J.T., and Milham, M.P. (2020). Towards a connectivity gradient-based frameworrk for reproducible biomarker discovery. bioRxiv

Huntenburg, J.M., Bazin, P.L., Goulas, A., Tardif, C.L., Villringer, A., and Margulies, D.S. (2017). A Systematic Relationship Between Functional Connectivity and Intracortical Myelin in the Human Cerebral Cortex. Cereb Cortex 27, 981-997.

Huntenburg, J.M., Bazin, P.L., and Margulies, D.S. (2018). Large-Scale Gradients in Human Cortical Organization. Trends Cogn Sci 22, 21-31.

Kabat-Zinn, J. (1990). Full catastrophe living: using the wisdom of your body and mind to face stress, pain, and illness. (New York, NY: Delacorte).

Kanske, P., Bockler, A., Trautwein, F.M., and 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.

Kernbach, J.M., Yeo, B.T.T., Smallwood, J., Margulies, D.S., Thiebaut de Schotten, M., Walter, H., Sabuncu, M.R., Holmes, A.J., Gramfort, A., Varoquaux, G., *et al.* (2018). Subspecialization within default mode nodes characterized in 10,000 UK Biobank participants. Proc Natl Acad Sci U S A 115, 12295-12300.

Kleckner, I.R., Zhang, J., Touroutoglou, A., Chanes, L., Xia, C., Simmons, W.K., Quigley, K.S., Dickerson, B.C., and Barrett, L.F. (2017). Evidence for a Large-Scale Brain System Supporting Allostasis and Interoception in Humans. Nat Hum Behav 1.

Klimecki, O.M., Leiberg, S., Ricard, M., and Singer, T. (2014). Differential pattern of functional brain plasticity after compassion and empathy training. Soc Cogn Affect Neurosci 9, 873-879.

Kok, B.E., and Singer, T. (2016). Effects of Contemplative Dyads on Engagement and Perceived Social Connectedness Over 9 Months of Mental Training: A Randomized Clinical Trial. JAMA Psychiatry.

Lamm, C., Decety, J., and Singer, T. (2011). Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. Neuroimage 54, 2492-2502.

Lutz, A., Mattout, J., and Pagnoni, G. (2019). The epistemic and pragmatic value of non-action: a predictive coding perspective on meditation. Curr Opin Psychol 28, 166-171.

Margulies, D.S., Ghosh, S.S., Goulas, A., Falkiewicz, M., Huntenburg, J.M., Langs, G., Bezgin, G., Eickhoff, S.B., Castellanos, F.X., Petrides, M., *et al.* (2016). Situating the default-mode network along a principal gradient of macroscale cortical organization. Proc Natl Acad Sci U S A 113, 12574-12579.

Menon, V. (2015). Salience Network. In Brain Mapping: An Encyclopedic Reference, A.W. Toga, ed. (Academic Press: Elsevier), pp. 597-611.

Menon, V., and Uddin, L.Q. (2010). Saliency, switching, attention and control: a network model of insula function. Brain Struct Funct 214, 655-667.

Mesulam, M.M. (1998). From sensation to cognition. Brain 121 (Pt 6), 1013-1052.

Murphy, C., Jefferies, E., Rueschemeyer, S.A., Sormaz, M., Wang, H.T., Margulies, D.S., and Smallwood, J. (2018). Distant from input: Evidence of regions within the default mode network supporting perceptually-decoupled and conceptually-guided cognition. Neuroimage 171, 393-401.

Murphy, C., Wang, H.T., Konu, D., Lowndes, R., Margulies, D.S., Jefferies, E., and Smallwood, J. (2019). Modes of operation: A topographic neural gradient supporting stimulus dependent and independent cognition. Neuroimage 186, 487-496.

Neff, K.D., and Germer, C.K. (2013). A pilot study and randomized controlled trial of the mindful self-compassion program. J Clin Psychol 69, 28-44.
Ochsner, K.N., and Lieberman, M.D. (2001). The emergence of social cognitive neuroscience. Am Psychol 56, 717-734.
Paquola, C., Benkarim, O., DeKraker, J., Lariviere, S., Frassle, S., Royer, J., Tavakol, S., Valk, S., Bernasconi, A., Bernasconi, N., *et al.* (2020a). Convergence of cortical types and functional motifs in the human mesiotemporal lobe. Elife 9.
Paquola, C., Bethlehem, R.A.I., and Bernhardt, B.C. (2020b). A moment of change: shifts in myeloarchitecture characterise adolescent development of cortical gradients. eLife.
Paquola, C., Vos De Wael, R., Wagstyl, K., Bethlehem, R.A.I., Hong, S.J., Seidlitz, J., Bullmore, E.T., Evans, A.C., Misic, B., Margulies, D.S., *et al.* (2019). Microstructural and functional gradients are increasingly dissociated in transmodal cortices. PLoS Biol 17, e3000284.
Park, B., Bethlehem, R.A.I., Paquola, C., Lariviere, S., Cruces, R.R., Vos De Wael, R., Consortium, N.i.P.N., Bullmore, E.T., and Bernhardt, B.C. (2020). Macroscale connectome manifold expansion in adolescence. bioRxiv
Pernet, C.R., Belov, N., Delorme, A., and Zammit, A. (2021). Mindfulness related changes in grey matter: a systematic review and meta-analysis. Brain Imaging Behav.
Pessoa, L. (2014). Understanding brain networks and brain organization. Phys Life Rev 11, 400-435.
Pinheiro, J.C., and Bates, D. (2000). Mixed-effect models in S and S-PLUS (Springer).
Power, J.D., Barnes, K.A., Snyder, A.Z., Schlaggar, B.L., and Petersen, S.E. (2012). Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. Neuroimage 59, 2142-2152.
Preston, S.D., and de Waal, F.B. (2002). Empathy: Its ultimate and proximate bases. Behav Brain Sci 25, 1-20; discussion 20-71.
Raz, G., Touroutoglou, A., Wilson-Mendenhall, C., Gilam, G., Lin, T., Gonen, T., Jacob, Y., Atzil, S., Admon, R., Bleich-Cohen, M., *et al.* (2016). Functional connectivity dynamics during film viewing reveal common networks for different emotional experiences. Cogn Affect Behav Neurosci 16, 709-723.
Rubinov, M., and Sporns, O. (2010). Complex network measures of brain connectivity: uses and interpretations. Neuroimage 52, 1059-1069.
Salzberg, D. (1995). Lovingkindness. The Revolutionary Art of Happiness. (Boston, MA: Shambala).
Saxe, R., and Kanwisher, N. (2003). People thinking about thinking people. The role of the temporo-parietal junction in "theory of mind". Neuroimage 19, 1835-1842.
Schaafsma, S.M., Pfaff, D.W., Spunt, R.P., and Adolphs, R. (2015). Deconstructing and reconstructing theory of mind. Trends Cogn Sci 19, 65-72.
Schaefer, A., Kong, R., Gordon, E.M., Laumann, T.O., Zuo, X.N., Holmes, A.J., Eickhoff, S.B., and Yeo, B.T.T. (2018). Local-Global Parcellation of the Human Cerebral Cortex from Intrinsic Functional Connectivity MRI. Cereb Cortex 28, 3095-3114.
Schilbach, L., Timmermans, B., Reddy, V., Costall, A., Bente, G., Schlicht, T., and Vogeley, K. (2013). Toward a second-person neuroscience. Behav Brain Sci 36, 393-414.
Schurz, M., Maliske, L., and Kanske, P. (2020a). Cross-network interactions in social cognition: A review of findings on task related brain activation and connectivity. Cortex.
Schurz, M., Radua, J., Aichhorn, M., Richlan, F., and Perner, J. (2014). Fractionating theory of mind: a meta-analysis of functional brain imaging studies. Neurosci Biobehav Rev 42, 9-34.
Schurz, M., Radua, J., Tholen, M.G., Maliske, L., Margulies, D.S., Mars, R.B., Sallet, J., and Kanske, P. (2020b). Toward a hierarchical model of social cognition: A neuroimaging meta-analysis and integrative review of empathy and theory of mind. Psychol Bull.

Schwarz, R.C. (1997). Internal familly systems therapy. (New York: Guilford).
Shine, J.M. (2020). The thalamus integrates the macrosystems of the brain to facilitate complex, adaptive brain network dynamics. Prog Neurobiol, 101951.
Shine, J.M., Aburn, M.J., Breakspear, M., and Poldrack, R.A. (2018). The modulation of neural gain facilitates a transition between functional segregation and integration in the brain. Elife 7.
Shine, J.M., Bissett, P.G., Bell, P.T., Koyejo, O., Balsters, J.H., Gorgolewski, K.J., Moodie, C.A., and Poldrack, R.A. (2016). The Dynamics of Functional Brain Networks: Integrated Network States during Cognitive Task Performance. Neuron 92, 544-554.
Shine, J.M., Breakspear, M., Bell, P.T., Ehgoetz Martens, K.A., Shine, R., Koyejo, O., Sporns, O., and Poldrack, R.A. (2019). Human cognition involves the dynamic integration of neural activity and neuromodulatory systems. Nat Neurosci 22, 289-296.
Shine, J.M., and Poldrack, R.A. (2018). Principles of dynamic network reconfiguration across diverse brain states. Neuroimage 180, 396-405.
Singer, T. (2006). The neuronal basis and ontogeny of empathy and mind reading: review of literature and implications for future research. Neurosci Biobehav Rev 30, 855-863.
Singer, T. (2012). The past, present and future of social neuroscience: a European perspective. Neuroimage 61, 437-449.
Singer, T., Kok, B.E., Bornemann, B., Zurborg, S., Bolz, M., and Bochow, C.A. (2016). The ReSource Project. Background, design, samples and measurements (2nd ed).
Singer, T., and Lamm, C. (2009). The social neuroscience of empathy. Ann N Y Acad Sci 1156, 81-96.
Singer, T., Seymour, B., O'Doherty, J., Kaube, H., Dolan, R.J., and Frith, C.D. (2004). Empathy for pain involves the affective but not sensory components of pain. Science 303, 1157-1162.
Smallwood, J., Turnbull, A., Wang, H.T., Ho, N.S.P., Poerio, G.L., Karapanagiotidis, T., Konu, D., McKeown, B., Zhang, M., Murphy, C., *et al.* (2021). The neural correlates of ongoing conscious thought. iScience 24, 102132.
Song, C., Kanai, R., Fleming, S.M., Weil, R.S., Schwarzkopf, D.S., and Rees, G. (2011). Relating inter-individual differences in metacognitive performance on different perceptual tasks. Conscious Cogn 20, 1787-1792.
Sormaz, M., Murphy, C., Wang, H.T., Hymers, M., Karapanagiotidis, T., Poerio, G., Margulies, D.S., Jefferies, E., and Smallwood, J. (2018). Default mode network can support the level of detail in experience during active task states. Proc Natl Acad Sci U S A 115, 9318-9323.
Tang, Y.Y., Holzel, B.K., and Posner, M.I. (2015). The neuroscience of mindfulness meditation. Nat Rev Neurosci 16, 213-225.
Tholen, M.G., Trautwein, F.M., Böckler, A., Singer, T., and Kanske, P. (2020). Functional magnetic resonance imaging (fMRI) item analysis of empathy and theory of mind. Hum Brain Mapp.
Tomasello, M. (1995). Joint atttention as social cognition. In Joint attentioon: Its origins and role in development, C. Moore, and P.J. Dunham, eds. (LawrenceErlbaum Associates, Inc.), pp. 103-130.
Trautwein, F.M., Kanske, P., Bockler, A., and Singer, T. (2020). Differential benefits of mental training types for attention, compassion, and theory of mind. Cognition 194, 104039.
Trautwein, F.M., Singer, T., and Kanske, P. (2016). Stimulus-Driven Reorienting Impairs Executive Control of Attention: Evidence for a Common Bottleneck in Anterior Insula. Cereb Cortex.
Turnbull, A., Karapanagiotidis, T., Wang, H.T., Bernhardt, B.C., Leech, R., Margulies, D., Schooler, J., Jefferies, E., and Smallwood, J. (2020). Reductions in task positive neural

systems occur with the passage of time and are associated with changes in ongoing thought. Sci Rep 10, 9912.
Turnbull, A., Wang, H.T., Murphy, C., Ho, N.S.P., Wang, X., Sormaz, M., Karapanagiotidis, T., Leech, R.M., Bernhardt, B., Margulies, D.S., *et al.* (2019a). Left dorsolateral prefrontal cortex supports context-dependent prioritisation of off-task thought. Nat Commun 10, 3816.
Turnbull, A., Wang, H.T., Schooler, J.W., Jefferies, E., Margulies, D.S., and Smallwood, J. (2019b). The ebb and flow of attention: Between-subject variation in intrinsic connectivity and cognition associated with the dynamics of ongoing experience. Neuroimage 185, 286-299.
Uddin, L.Q. (2015). Salience processing and insular cortical function and dysfunction. Nat Rev Neurosci 16, 55-61.
Valk, S.L., Bernhardt, B.C., Trautwein, F.M., Bockler, A., Kanske, P., Guizard, N., Collins, D.L., and Singer, T. (2017). Structural plasticity of the social brain: Differential change after socio-affective and cognitive mental training. Sci Adv 3, e1700489.
Valk, S.L., Xu, T., Margulies, D.S., Kharabian Masouleh, S., Paquola, C., Goulas, A., Kochunov, P., Smallwood, J., Yeo, B.T., Bernhardt, B.C., and Eickhoff, S.B. (2020). Shaping Brain Structure: Genetic and Phylogenetic Axes of Macro Scale Organization of Cortical Thickness. Sci Adv.
Van Essen, D.C., Smith, S.M., Barch, D.M., Behrens, T.E., Yacoub, E., Ugurbil, K., and Consortium, W.U.-M.H. (2013). The WU-Minn Human Connectome Project: an overview. Neuroimage 80, 62-79.
Vos de Wael, R., Benkarim, O., Paquola, C., Lariviere, S., Royer, J., Tavakol, S., Xu, T., Hong, S.J., Valk, S.L., Misic, B., *et al.* (2020). BrainSpace: a toolbox for the analysis of macroscale gradients in neuroimaging and connectomics datasets. Nat Commun Biology.
Vos de Wael, R., Lariviere, S., Caldairou, B., Hong, S.J., Margulies, D.S., Jefferies, E., Bernasconi, A., Smallwood, J., Bernasconi, N., and Bernhardt, B.C. (2018). Anatomical and microstructural determinants of hippocampal subfield functional connectome embedding. Proc Natl Acad Sci U S A 115, 10154-10159.
Wittchen, H.U., and Pfister, H. (1997). Diagnostisches Expertensystem für psychische Störungen (DIA-X) (Frankfurt: Swets & Zeitlinger).
Wittchen, H.U., Zaudig, M., and Fydrich, T. (1997). SKID-Strukturiertes Klinisches Interview für DSM-IV. Achse I und II (Göttingen: Hogrefe).
Worsley, K., Taylor, J.E., Carbonell, F., Chung, M.K., Duerden, E., Bernhardt, B.C., Lyttelton, O.C., Boucher, M., and 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.
Worsley, K.J., Andermann, M., Koulis, T., MacDonald, D., and Evans, A.C. (1999). Detecting changes in nonisotropic images. Hum Brain Mapp 8, 98-101.
Xu, T., Nenning, K., Schwartz, E., Hong, S.J., Vogelstein, J.T., Fair, D.A., Schroeder, C.E., Margulies, D.S., Smallwood, J., Milham, M.P., and Langs, G. (2020). Cross-species Functional Alignment Reveals Evolutionary Hierarchy Within the Connectome. Neuroimage.
Yarkoni, T., Poldrack, R.A., Nichols, T.E., Van Essen, D.C., and Wager, T.D. (2011). Large-scale automated synthesis of human functional neuroimaging data. Nat Methods 8, 665-670.
Yeo, B.T., Krienen, F.M., Sepulcre, J., Sabuncu, M.R., Lashkari, D., Hollinshead, M., Roffman, J.L., Smoller, J.W., Zollei, L., Polimeni, J.R., *et al.* (2011). The organization of the human cerebral cortex estimated by intrinsic functional connectivity. J Neurophysiol 106, 1125-1165.
Zaki, J., Weber, J., Bolger, N., and Ochsner, K. (2009). The neural bases of empathic accuracy. Proc Natl Acad Sci U S A 106, 11382-11387.