Supplementary Material for Mennes et al., *The extrinsic and intrinsic functional architectures of the human brain are not equivalent.*

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1 Methods

1.1 Participants and Task Paradigms

1.1.1 Participants

We applied our analyses to three task datasets that differed with respect to the task paradigm and participant sample. All participants were adults without a history of psychiatric or neurological illness as confirmed by psychiatric assessment. Written informed consent was obtained prior to participation as approved by the institutional review boards of New York University (NYU) and the NYU School of Medicine.

1.1.2 Eriksen Flanker Task

Twenty-six participants (mean age 28.5 ± 8.5 years, 11 males) completed two 5-minute runs of a slow event-related Eriksen Flanker task (inter-trial interval varied between 8 and 14 s with mean = 12 s). On each trial, participants had to indicate the direction of a central arrow in an array of 5 arrows. In congruent trials the flanking arrows pointed in the same direction as the central arrow (e.g., > > > > >), while in incongruent trials the flanking arrows pointed in the opposite direction (e.g., > > < > >). Each run contained 12 congruent and 12 incongruent trials, presented in a pseudorandom order, and the two task runs were always administered consecutively. Participants responded using the index- and middle finger of the right hand. These data have been reported in previous studies by our lab (Kelly et al. 2008; Mennes et al. 2010; Mennes et al. 2011) and are publically available via http://openfmri.org/database.html.
1.1.3 Simon Stimulus Response Compatibility Task

Twenty-one participants completed two 5-minute runs of a rapid event-related Simon stimulus-response compatibility task (mean age: 30.5±7.3yrs, 12 males). On each trial, participants were asked to maintain fixation on a cross in the middle of the screen and to indicate whether a colored diamond that was presented to the left or right of the fixation cross was green (left-hand button-press) or red (right-hand button-press) in color. In congruent trials, the color of the diamond was compatible (consistent) with its spatial location (i.e., a green diamond appearing on the left side of the screen or a red diamond appearing on the right). In incongruent trials, the color of the diamond was incompatible with its spatial location (i.e., a red diamond appearing on the right side of the screen or a green diamond appearing on the right). Each run comprised 48 congruent, 48 incongruent and 24 dummy (fixation-only) trials presented in a predetermined order, with a mean inter-trial interval of 3.125 seconds (range 2.5 – 10s). These data are publically available via http://openfmri.org/database.html.

1.1.4 Risky Decision Making Task

Twenty-four participants (mean age: 29.9 ± 8.5yrs, 16 males) completed four 7.5-minute runs of a rapid event-related Risky decision making task in which they earned points by betting on a “wheel of fortune”. At the beginning of each trial, participants were presented with a wheel that was divided into two sections, the ratio of which corresponded to one of three levels of probability: 6:1, 5:2, and 4:3. The two sections were either worth the same (500/500) or different (100/900) number of points, corresponding to no-risk (a “win” would occur regardless of the decision) or risky conditions, respectively. Rewards were either large (500/500 or 100/900) or small (50/50 or 10/90). After choosing a section of the wheel on which to place their “bet” (participants had 4s to make their decision) the wheel was “spun” (for either 0.5s or 7s), and the
participant was informed of the outcome (feedback was presented for 2.5s). At the end of the task, points were converted into prize money. For the purpose of the present analyses, we modeled all decision and feedback (outcome) events regardless of the particular condition (i.e., probability, risk, or reward size). Each run comprised 42 decision and feedback trials, as well as 10-12 dummy trials. The mean inter-trial interval was 10.8s (range: 7 – 23s).

1.1.5 Resting state Scans

All participants completed a brief (6.5 min) resting state scan during which they were asked to relax while keeping their eyes open. The order of the resting state and task scans was counterbalanced across participants.

A subset of 21 participants (including six participants who did not complete any task scans) completed three resting state scans. Two scans were completed in the same session (i.e., ~45 minutes apart), while the third scan was completed 5-11 months prior to the first two. Using this “test-retest” dataset we were able to index resting state scan iFC-iFC similarity within participants over both short (45 minutes between scans) and long (5-16 months between scans) intervals. These data have been published in several test-retest reliability studies by our lab (Shehzad et al. 2009; Zuo et al. 2010; Zuo et al. 2010) and are also publically available via http://fcon_1000.projects.nitrc.org/fcpClassic/FcpTable.html

1.1.6 Participant overlap between task datasets

In total, task data were collected from 50 unique participants. Twenty-one participants completed both the Eriksen Flanker and Risky Decision-Making tasks, but of the 21 participants who performed the Simon task none completed either the Eriksen Flanker or Risky Decision-
Making tasks. Five participants completed only the Eriksen Flanker task, while 3 completed only the Risky Decision-Making task.

1.1.7 Participant overlap between task datasets and test-retest resting state dataset

Of the 21 participants who completed the test-retest resting state scans, 6 did not complete any of the task scans. Of the 15 participants who also completed a task, 2 completed the Eriksen Flanker task, 7 completed the Simon task and 6 completed both the Risky Decision-Making and the Eriksen Flanker tasks.
1.2 Data acquisition and image preprocessing

1.2.1 Data acquisition

All scans were acquired using a standard Siemens head coil on a Siemens Allegra 3.0T scanner. Functional MRI scans were collected as contiguous echo planar imaging (EPI) whole-brain volumes (TR = 2000 ms; TE = 30 ms; flip angle = 80°; 40 slices: matrix = 64 × 64; FOV = 192 mm; acquisition voxel size = 3 × 3 × 4 mm). 146 volumes were collected in each of the Eriksen Flanker runs, 151 volumes in each of the Simon runs and 230 in each of the Risky Decision-Making task runs. The resting state scan comprised 197 contiguous EPI volumes (TR = 2000 ms; TE = 25 ms; flip angle = 90°; 39 slices: matrix = 64 × 64; FOV = 192 mm; acquisition voxel size = 3 × 3 × 3 mm). For spatial normalization and localization, we obtained a high-resolution T1-weighted magnetization prepared gradient echo sequence for each participant (MPRAGE: TR = 2500 ms; TE = 4.35 ms; TI = 900 ms; flip angle = 8°; 176 slices: FOV = 256mm).

1.2.2 Image preprocessing

All task scans were processed as follows: Concatenation of all runs, slice timing correction for interleaved acquisition (using Fourier-space time-series phase-shifting), motion correction (by aligning each volume to the 8th image using Fourier interpolation) and despiking (detection and reduction of extreme time series outliers) were carried out using AFNI (http://afni.nimh.nih.gov/afni/). Despiking was not done for the Risky Decision-Making task due to computational limitations. Further preprocessing was performed using FSL (www.fmrib.ox.ac.uk) and comprised spatial smoothing using a Gaussian kernel of FWHM 6mm, mean-based intensity normalization of all volumes by the same factor (i.e., all volumes are
scaled by the same amount), and temporal filtering using both a high-pass (Gaussian-weighted least-squares straight line fitting, with sigma = 100.0 s) and low-pass filter (Gaussian-weighted least-squares straight line fitting, with sigma = 1 s), keeping signal between 0.01 and 1 Hz.

After preprocessing we regressed out signal associated with several nuisance covariates from the preprocessed images. For all task scans we included signal associated with white matter, cerebrospinal fluid, and six motion parameters in a participant-level regression analysis (FSL FEAT). The 4-D residual time series obtained after removing the nuisance covariates were used for the subsequent participant-level analyses.

The resting state scans were preprocessed similarly except for the temporal filter where the bandpass was limited to 0.095 – 0.1 Hz. In addition we also regressed out signal associated with a global time series, generated by averaging across all voxels in the brain.

Registration of each participant’s high-resolution anatomical image to a common stereotaxic space (the Montreal Neurological Institute 152-brain template (MNI152); 3×3×3mm resolution) was accomplished using a two-step process (Andersson et al. 2007). First, a 12 degrees of freedom linear affine transformation was computed using FLIRT (Jenkinson and Smith 2001; Jenkinson et al. 2002). Subsequently, the registration was refined using FNIRT nonlinear registration (Andersson et al. 2007).

1.2.3 Participant-level task-based analyses: beta value time series

For each participant in each task we conducted a participant-level multiple regression, modeling trials as individual predictors (Rissman et al. 2004). This allowed us to construct a time series of estimated trial-wise evoked responses (beta values), which was then used to calculate voxel-wise eFC maps. Next to trial-wise predictors each participant’s GLM included a covariate coding for task run. Only correctly answered trials were modeled and compared to all remaining BOLD activity (referred to as “baseline”). Each trial’s beta image was registered to 3mm.
MNI152 standard space. For the Eriksen Flanker this procedure resulted in beta values for each of 24 congruent and 24 incongruent trials if all trials were answered correctly.

To account for BOLD signal overlap inherent to the rapid-event related design of the Simon and Risky Decision-Making task we optimized response estimation for both tasks by randomly grouping 4 trials of the same type into 1 predictor. Each trial was not included more than once. In the Simon task we randomly grouped trials counterbalancing for the previously presented trial. Specifically, we randomly split each participants 96 congruent trials into 24 trial groups each including 4 congruent trials, 2 of which were preceded by a congruent trial and 2 of which were preceded by an incongruent trial. The same was done for all incongruent trials. After the participant-level GLM this resulted in beta values for each of 24 congruent and 24 incongruent ‘trials’. In the Risky Decision-Making task beta values were obtained for 42 decision and 42 feedback predictors, each including 4 randomly selected decision or feedback events.

### 1.3 iFC-eFC relationship

#### 1.3.1 Participant-level computations

We defined iFC (intrinsic functional connectivity) as the temporal correlation between voxels’ resting state fMRI time series. Likewise, we defined eFC (extrinsic functional connectivity) as the correlation between voxels’ task-evoked hemodynamic responses across trials (eFC is also referred to as co-activation). Only voxels that had a probability of being gray matter exceeding 25% in the FSL avg152 gray matter tissueprior were included in our analyses, effectively including over 55000 voxels in each calculation.
After registering each participant’s 4-D residual resting state images to 3mm MNI standard space, we generated each voxels’ iFC map by correlating its resting state time series with that of every other gray matter voxel. Similarly, we calculated the eFC map for each gray matter voxel, by correlating each voxel’s beta value time series quantifying the magnitude of task-evoked responses with the beta value time series of every other gray matter voxel.

Subsequently, for each participant, we calculated the spatial correlation between each voxel’s iFC and eFC map. The iFC-eFC correlations were z-transformed using the Fisher r-to-z transformation to improve normal distribution. This analysis resulted in a map for each participant that indexed for every voxel how similar its pattern of task-evoked functional interactions (eFC map) was to its intrinsic functional architecture (iFC map).

1.3.2 Trial-types and ‘tight’ comparisons

eFC maps were calculated both across congruent and incongruent trials (congruent + incongruent > baseline) as well as for each trial type separately in the Eriksen Flanker and Simon tasks. In the Risky Decision-Making task we calculated eFC maps for the decision and feedback trials separately. The beta value time series for each of these trial types were all of ‘broader’ trial > baseline comparisons (e.g., congruent > baseline). In addition we also calculated eFC maps for ‘tight’ comparisons. We calculated eFC maps for Incongruent > Congruent in the Eriksen Flanker and Simon task. Specifically, for each voxel, we subtracted the eFC map obtained for congruent trials from the eFC map obtained for incongruent trials before calculating the correlation with that participant’s and voxel’s iFC map.
1.3.3 Group-level analyses

To identify those voxels whose iFC-eFC correlation was significantly different from 0 across participants we did group-level analyses for every dataset using FSL FEAT. The resulting zstat maps were corrected for multiple comparisons using Gaussian Random Field theory (Z > 2.3, p < 0.05 corrected).

Overall mean iFC-eFC relationships were compared between datasets in a one-way ANOVA including dataset (Eriksen Flanker, Simon, Risky Decision-Making, Short-, and Long Test-retest) as factor. Tukey HSD tests determined the significance of post-hoc pair-wise comparisons (p<0.05).

1.3.4 Hierarchical Classification

To characterize the regional differences observed in the strength of the iFC-eFC correlations, we classified voxels according to a previously established functional hierarchy (Mesulam 2000). Voxels were classified according to the Harvard-Oxford Structural Atlas (included with FSL) prior to classification according to the functional hierarchy. Six hierarchical classes were included: subcortical, limbic, paralimbic, primary sensory-motor, unimodal association and hetermodal association areas. We subsequently compared the mean iFC-eFC relationship obtained for each hierarchical classification in a one-way ANOVA including classification (subcortical, limb, paralimbic, primary sensory-motor, unimodal and hetermodal) as factor. Tukey HSD tests determined the significance of post-hoc pair-wise comparisons (p<0.05).
1.3.5 Generalizability across datasets

To assess the generalizability of the topography observed in the strength of the iFC-eFC relationships, we calculated the spatial correlation between the iFC-eFC correlation maps obtained for each dataset.

In addition, we examined differences in iFC-eFC strength between all task datasets by conducting a whole-brain one-way ANOVA (FSL FEAT) across participants including all task datasets as the factor (Eriksen Flanker, Simon, Decision and Feedback). To account for differences in the overall mean iFC-eFC correlation between datasets (see Fig. 1) we entered each participant’s overall mean iFC-eFC correlation as covariate in the model. The resulting zstat maps were corrected for multiple comparisons using Gaussian Random Field theory (Z > 2.3, p < 0.05 corrected).

1.3.6 Dice Coefficient

We investigated whether the iFC-eFC relationships were possibly biased by a voxel’s network size. For instance, a voxel in PCC is significantly correlated with a larger number of other voxels (i.e., the default network) than a voxel in motor cortex. This phenomenon might have biased our analyses towards the detection of stronger iFC-eFC relationships for voxels within larger networks. To address this issue, we conducted a secondary analysis computing iFC-eFC correspondence for every voxel using the Dice coefficient. The Dice coefficient indexes the spatial overlap between iFC and eFC maps and is calculated as twice the number of overlapping voxels divided by the union of both maps (i.e., [(2*(iFC ∩ eFC))/(iFC ∪ eFC)]). Only significantly positively connected voxels in the iFC and eFC maps were considered. The p < 0.05 significance cut-off was determined using the degrees of freedom of the data time-series corrected for the band pass filter (r > 0.32 for iFC, r > 0.3 for Eriksen Flanker and Simon eFC, r
> 0.22 for Risky Decision Making).
2 Results

2.1 Task Activation Maps

Supplementary Figure 1. Task-evoked activation and deactivation patterns for the specific contrasts in each dataset. In contrast to the regression model including each trial as a separate variable that was used for eFC calculation, these task-evoked activity patterns were obtained
through conventional multiple regression, grouping trials according to type into variables. For the flanker and Simon task the con + incon map illustrates task-evoked activity observed for the congruent + incongruent > baseline contrast. It should be noted that the task activation maps for the Simon task exhibit rather weak group-level activation. Additionally the incongruent > congruent contrast exhibits a limited number of significant regions for the Eriksen Flanker as well as the Simon task. However, weaker group-level activation maps do not affect our results, as all iFC-eFC calculations were done at the individual participant level. High iFC-eFC correlations are obtained by the fact that the variation in task activation maps (in turn reflected in the eFC map) is at least to some degree reflected in the iFC maps obtained from the resting state scan.
2.2 *The topography of iFC-eFC relationships generalized across samples and paradigms*

The strong correlations reported in Supplementary Table 1 support the visual observation that the topography of iFC-eFC relationships was highly similar across the samples and paradigms included in our analyses (see also Fig. 2 in the main text).

**Supplementary Table 1.** Between-dataset correlations of the voxel-wise iFC-eFC relationships.

<table>
<thead>
<tr>
<th></th>
<th>Flanker</th>
<th>Simon</th>
<th>Decision</th>
<th>Feedback</th>
<th>Short TRT</th>
<th>Long TRT</th>
</tr>
</thead>
<tbody>
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<td></td>
<td>0.85</td>
<td>0.87</td>
<td>0.89</td>
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</tr>
<tr>
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<tr>
<td>Long TRT</td>
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<td></td>
<td>0.95</td>
</tr>
</tbody>
</table>
2.3 *Core regions of the Default and Task-Positive Networks exhibited the strongest iFC-eFC correlations*

**Supplementary Figure 2.** Core regions of the frequently described “default” and “task-positive” networks exhibited the strongest iFC-eFC correlations. **A.** Default intrinsic functional connectivity network (n=56, Z > 2.3, p < 0.01). **B.** Task-positive intrinsic functional connectivity network (n=56, Z > 2.3, p < 0.01). **C.** Regions showing the 10% strongest iFC-eFC correlations in the Simon dataset. In practice, the mean iFC-eFC correlation map obtained for the Simon dataset was thresholded at r>0.26. **D.** Intersection of voxels showing the strongest iFC-eFC correlations and membership in either the default or task-positive intrinsic functional connectivity networks. For a similar approach see Vaishnavi et al. (2010). The default and task-positive intrinsic functional connectivity network maps were obtained through resting state...
functional connectivity analyses using seed ROI’s combined into one mask prior to seed

timeseries extraction. For the default network we included: medial prefrontal cortex [-1,47,-4],
posterior cingulate/precuneus [-5, -49, 40], and lateral parietal cortex [-45, -67, 36]. For the task-
positive network we included: intraparietal sulcus [-25, -57, 46], middle temporal region [MT+, -
45, -69, -2], and the right frontal eye field region of the precentral sulcus [25, -13, 50]. We
included all participants unique to one of the 4 included samples. As such, a total of 56
participants were included in a group-level analysis.
2.4 *Regional differences in iFC-eFC adhere to a functional hierarchy*

In order to characterize the regional differences in iFC-eFC correlations, we classified regions according to a previously established functional hierarchy (Mesulam 2000). Subcortical and limbic areas exhibited the weakest iFC-eFC relationships, followed by slightly stronger relationships for primary sensory-motor areas. In contrast, the strongest iFC-eFC relationships were observed for unimodal and heteromodal association areas as well as paralimbic areas (Supplementary Fig. 4).

**Supplementary Figure 3.** Classification of the iFC-eFC correlations in the Simon dataset according to the functional hierarchy described by Mesulam (2000). Subcortical and limbic areas exhibited significantly lower iFC-eFC relationships than paralimbic, and unimodal and heteromodal association areas. iFC-eFC relationships observed for voxels in primary sensory-motor areas were significantly lower than those observed for heteromodal association areas, but did not differ from all other functional classes. * p < 0.05; ns: not significant. Bars depict mean + standard error.
Supplementary Figure 4. Functional hierarchical classification of the mean iFC-eFC correlations obtained in each dataset. For all datasets, subcortical and limbic areas exhibited lower iFC-eFC relationships compared to the other functional classes (primary sensory-motor areas, paralimbic, unimodal and heteromodal association areas). Bars depict mean iFC-eFC correlation + standard error.
2.5 Individual Trial Types in Flanker and Simon Dataset

**Supplementary Table 2.** Within and between-dataset correlations of the iFC-eFC patterns obtained for the different trial types included in the flanker and Simon task. Green: within-dataset correlations comparing the iFC-eFC relationships obtained for each trial type in the flanker task. Orange: within-dataset correlations comparing the iFC-eFC relationships obtained for each trial type in Simon task. Yellow: between-dataset correlations comparing the iFC-eFC relationships obtained for each trial type in the flanker and Simon task. Overall: congruent + incongruent > baseline. Congruent: congruent > baseline. Incongruent: incongruent > baseline. Incon > Con: incongruent > congruent.

<table>
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<tr>
<th>Flanker vs. Simon</th>
<th>Overall</th>
<th>Congruent</th>
<th>Incongruent</th>
<th>Incon &gt; Con</th>
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<td><strong>Flanker</strong></td>
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<tr>
<td><strong>Simon</strong></td>
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<tr>
<td>Overall</td>
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<td>Congruent</td>
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</table>
2.6 *Between task differences in iFC-eFC strength*

Supplementary Figure 5. A limited number of regions exhibited a main effect of task dataset on their iFC-eFC correlations. Bar plots show the data for the clusters identified on the surface maps. Of note, these clusters were found in areas that showed strong iFC-eFC correlations in each dataset (see Figure 2 in the main text), indicating that the between-dataset differences observed in this analysis are differences in magnitude rather than topography.
2.7 **Signal-to-Noise Ratio did not explain our results, fALFF did**
Supplementary Figure 6. Across participant mean voxel-wise SNR values calculated for the resting state scan (blue, top row) were moderately correlated with the mean iFC-eFC relationship ($r=0.21 – 0.27$). Mean voxel-wise SNR values calculated for the task-based beta time series (green, middle rows) did not correlate with the mean iFC-eFC relationship ($r=-0.04 – 0.06$). T-score maps indexing the difference across participants between the resting state SNR and SNR based on the task-based beta time series also correlated moderately with the mean iFC-eFC relationship (range: 0.16 – 0.25; yellow, second to last row). Lower t-scores indicated higher task-based SNR relative to the resting state SNR. This result confirms that lower task-based SNR values were not contributing to weak iFC-eFC relationships as regions exhibiting higher SNR values for the task-based time series exhibited weaker iFC-eFC relationships. In contrast to the SNR results, resting state based mean fALFF values (red, bottom row) correlated strongly with the mean iFC-eFC relationship ($r=0.58 – 0.66$). SNR values were z-transformed within participants before calculating across participant means. Supplementary Table 3 lists the correlation values for the plots shown here.
**Supplementary Table 3.** Correlations between the mean iFC-eFC maps for each sample and the SNR, t-score or fALFF maps. Correlations correspond to the plot shown in Supplementary Figure 6.

<table>
<thead>
<tr>
<th></th>
<th>Flanker</th>
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<tr>
<td>Resting state SNR</td>
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<td>Task-based beta time series SNR incongruent vs. congruent</td>
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<td>-0.06</td>
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<tr>
<td>t-scores</td>
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<tr>
<td>fALFF</td>
<td>0.64</td>
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### 2.8 Spatial overlap between networks did not explain our results

As shown in Supplementary Figure 7, the topography of Dice coefficients obtained for every voxel was highly similar to the iFC-eFC topography obtained through functional connectivity (i.e. correlation) analyses. As described above, the Dice coefficient quantified the spatial overlap between significant iFC and eFC obtained for every voxel. The Dice results indicate that the size or spatial extent of a voxel’s iFC and eFC networks could not explain our results. In fact, the similarity between the Dice results and the results obtained through correlating the full iFC and eFC patterns (see Supplementary Table 3) suggests that regions that show a poor iFC-eFC correlation also show poor spatial overlap between their intrinsic and evoked functional connectivity networks (i.e., significantly connected voxels).
Supplementary Figure 7. Mere spatial overlap between significant iFC and eFC confirmed the topography observed for iFC-eFC correlations. Surface maps show the Dice coefficient, indexing the spatial overlap between each voxel’s significant iFC and eFC. All surface maps are scaled identically. The heat-map illustrates the between-dataset correlation of mean Dice maps. All correlations exceeded $r=0.7$. 
Supplementary Table 4. Between-dataset correlations of the voxel-wise spatial iFC-eFC overlap indexed by the Dice coefficient. Correlations on the bottom row correlate the Dice results with the iFC-eFC correlations reported as main results.

<table>
<thead>
<tr>
<th></th>
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<th>Long TRT</th>
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<td>iFC-eFC vs. Dice</td>
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2.9 Global signal regression did not influence the iFC-eFC topography
Supplementary Figure 8A. Global signal regression applied during preprocessing of the resting state scan influenced the strength, but not the topography of the iFC-eFC correlations. Surface plots show the topography of the mean iFC-eFC correlations across participants for analyses with (left) and without (right) global signal regression during preprocessing of the resting state scan. Scatterplots on the right illustrate the spatial correlation between the iFC-eFC correlations obtained with and without global signal regression during preprocessing of the resting state scan. These results indicate that not applying global signal regression during preprocessing of the resting state scan resulted in overall higher iFC-eFC correlations, yet the spatial topography was almost completely preserved.
Supplementary Figure 8B. Global signal regression applied during processing of the resting state scan did not alter the functional hierarchy observed in the iFC-eFC relationship. Bar graphs illustrate mean iFC-eFC correlations observed for each task dataset. The graphs on the left show the hierarchy for the analyses that included global signal regression on the resting state scan (see also Supplementary Figure 4). The graphs on the right show results for the analyses without global signal regression for the resting state scan. Of note, global signal regression was not applied during processing of any of the task scans. Comparing the graphs with global signal regression to those showing the results without global signal regression, it is clear the functional hierarchy observed in the iFC-eFC relationship was preserved for each dataset. However, not applying global signal regression resulted in slightly higher iFC-eFC correlations.
References

http://www.fmrib.ox.ac.uk/analysis/techrep/.


