Assessing the Function of the Fronto-Parietal Attention Network: Insights from Resting-State fMRI and the Attentional Network Test

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Abstract: In the recent past, various intrinsic connectivity networks (ICN) have been identified in the resting brain. It has been hypothesized that the fronto-parietal ICN is involved in attentional processes. Evidence for this claim stems from task-related activation studies that show a joint activation of the implicated brain regions during tasks that require sustained attention. In this study, we used functional magnetic resonance imaging (fMRI) to demonstrate that functional connectivity within the fronto-parietal network at rest directly relates to attention. We applied graph theory to functional connectivity data from multiple regions of interest and tested for associations with behavioral measures of attention as provided by the attentional network test (ANT), which we acquired in a separate session outside the MRI environment. We found robust statistical associations with centrality measures of global and local connectivity of nodes within the network with the alerting and executive control subfunctions of attention. The results provide further evidence for the functional significance of ICN and the hypothesized role of the fronto-parietal attention network. *Hum Brain Mapp* 35:1700–1709, 2014. © 2013 Wiley Periodicals, Inc.

Key words: resting state fMRI; functional connectivity; cognitive neuroscience

INTRODUCTION

The human brain is always buzzing and humming. Even in the absence of any specific task condition (a state which is confusingly labeled resting state) the brain is not at rest, but shows a strong degree of spontaneous activity.

An important feature of this activity is that it is by no means random. Different brain regions show a high coherence in their temporal fluctuations (i.e. functional connectivity; Friston et al., 1993) which has led to the hypothesis that the brain forms intrinsic connectivity networks (ICN). The term ICN describes a set of brain regions that are functionally interconnected (i.e., a network based on functional connectivities), even when the brain is not probed by external stimulation. Thus, the activity is not a reaction to some sort of task but intrinsically generated by the brain itself. Using different methodological approaches to functional connectivity data at least seven ICNs have been isolated that show a high degree of stability across subjects and time [Beckmann et al., 2005; Damoiseaux et al., 2006; DeLuca et al., 2008; van den Heuvel et al., 2008].

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Of these ICNs, the fronto-parietal attention network (FPAN) seems of special relevance for cognitive processes. The FPAN comprises hubs in the intraparietal sulcus, the orbital gyrus, the supplementary and pre-supplementary motor areas, the anterior insula, the ventral occipital cortex, the dorsolateral prefrontal cortex, the inferior parietal lobules and the frontal eye field [Fox et al., 2005; Fox et al., 2006; Toro et al., 2008]. In the literature there is no consensus whether the FPAN is a bilateral network spanning both hemispheres or if there are two lateralized FPANs [Beckmann et al., 2005; De Luca et al., 2006; Damoiseaux et al., 2006; for review see van den Heuvel and Hulshoff Pol, 2010]. Inconsistencies may arise due to the facts that the definition of networks is based on similarities and dissimilarities between blood oxygen level dependent (BOLD) time series, and that no data-driven consensus for setting analysis parameters has been reached yet. Irrespective of lateralization issues, brain regions involved in the FPAN show an increase in activation to external stimulation, especially during tasks that place demands on working memory and attention [Cabeza and Nyborg, 2000; Corbetta and Shulman, 2002; Fan et al., 2005]. This observation has inspired the term “task-positive” network for the FPAN and—from a functional point of view—a hypothesized implication for attentional performance [Fox et al., 2005, Vincent et al., 2008; Toro et al., 2008].

Most studies aiming at the psychological relevance of ICNs have focused on activations and deactivations of the networks’ hub regions during task conditions, while only a few have examined the influence of experimental manipulations on functional connectivity during rest [Andrews-Hannah et al., 2000; Fransson, 2005]. Another approach to the functional role of ICNs at rest is the examination of covariation between connectivities within an ICN and a relevant psychological variable acquired outside the MRI environment. This approach has been successfully applied to other ICNs [e.g., Liemberg et al., 2012; Sheng et al., 2010; Seeley et al., 2007]. For the FPAN, however, such evidence is scarce. In the present study, we seek to fill this gap by relating connectivity within the FPAN to cognitive ability in the domain of attention because this is the proposed role of the FPAN in cognition.

Attention refers to the prioritized processing of information in the face of other information competing for limited cognitive resources [Cowan, 1999; Fan et al., 2009]. Three different attentional functions are commonly distinguished [Posner and Petersen, 1990]. Alerting, as the establishment of a mental state of heightened vigilance in preparation for an upcoming stimulus. Orienting, as the capability of assigning attentional resources to a stimulus or a location in space to select this information for further processing. And executive control, as the third attentional function that becomes necessary once available information elicits inappropriate behavioral responses which conflict with present intentions. In this case, executive control biases the information processing in favor of a less dominant but more appropriate behavior. These three functions are

thought to be independent from each other [Fan et al., 2002], although newer evidence has shown subtle interactions between the three systems [Fan et al., 2009]. The attentional network test [ANT; Fan et al., 2002] is an assessment tool to measure the efficiency of the three functions on a behavioral level in the same individual at the same time. Neuroimaging studies with the ANT have shown that all three attentional functions cannot be localized in precisely circumscribed brain regions but require contributions of many distributed sites [Fan et al., 2005]. The finding that remote brain regions form neural networks during attentional task performances and the fact that some of these brain regions contribute to an intrinsic connectivity network suggest a possible relationship between the FPAN and task performance in the ANT.

An elegant means to quantify individual differences within an ICN is the application of graph theoretical measures to resting-state time-series from multiple regions of interest [Liu et al., 2010]. Mathematically, a graph is an abstract representation of a set of nodes where some or all of these nodes are interconnected by links. Graph theory has been successfully applied to functional imaging data by defining regions of interest as nodes and functional connectivities between the nodes as connecting links [Archard et al., 2006; Braun et al., 2012; van den Heuvel et al., 2008; for review see van den Heuvel and Hulshoff Pol, 2008]. In graph theory, a node’s centrality expresses its importance in the network. Different centrality measures that capture unique information about the network structure have been proposed [Zuo et al., 2012]. Degree centrality (DC) of a node reflects the number and strength of links that connect to the node and is a measure of how well the node is locally embedded in the network. Eigenvector centrality (EC) assigns a value to each node that describes how well the node is connected to other nodes that are themselves central in the network. Betweenness centrality (BC) of a node reflects how well the node is globally embedded in the network. BC quantifies the probability that the node lies on a randomly chosen shortest path between a randomly chosen pair of nodes and therefore represents how much of a switch point the node is between different parts of the network. To illustrate these centrality measures just picture yourself in a social network: DC describes the mere amount of friends you have, EC describes to what degree your friends have many friends themselves, and BC describes to what degree randomly chosen people in the network know each other through you. From that perspective it should become clear that DC represents a more local measure because it describes the amount of direct connectivity of a node of interest to other nodes, BC represents a more global measure because it integrates the relationship between a node of interest and all connections within the network, and EC represents a measure of intermediate connectivity because it covers the connections of those nodes connected to a node of interest.

In the present study, we apply all three centrality measures to functional connectivity data from regions of

interest that delineate the FPAN and relate these measures to the efficiency of attentional networks in a between-subject design. We chose centrality measures as the main graph analytic metrics because their usefulness in individual differences analyses has been proven previously [Liu et al., 2010]. Furthermore, centrality measures allow for conclusions on the relative importance of single nodes to a network and can therefore establish links between single regions in the FPAN and attentional task performance. The use of the term “attention network” in the literature is mainly based on evidence that the FPAN’s nodes are jointly activated during attentional tasks. Finding a relationship between properties of the FPAN in the resting brain and behavioral indices of attentional capability would provide more direct evidence—as opposed to the observed joint activation during task conditions—that the FPAN at rest plays a role in attention.

METHOD

Participants

Resting state fMRI data were collected from $N=23$ (males $n=2$, females $n=21$; age $M=21.74$, $SD=5.24$) participants after obtaining their informed written consent. All participants were free of any psychiatric or neurological condition as assessed by a screening questionnaire and had no contraindications to MRI. The study protocol was in accordance with the Declaration of Helsinki and approved by the local medical ethics committee of the University Hospital Bonn.

Behavioral Task

After completion of the fMRI scan, the participants’ attentional abilities were assessed by means of the Attentional Network Test (ANT). The ANT is described in detail elsewhere [Fan et al., 2002]. Briefly, participants were confronted with five horizontal lines that were either presented above or below a central fixation cross on a 15-inch (38.1 cm) computer screen. The line in the middle had arrowheads pointing either to the left or to the right and the participants’ task was to indicate as fast and accurately as possible the direction of the arrowhead by pressing a button on a computer keyboard. Three different manipulations of this procedure were realized to measure the three attentional functions: In some of the trials, a little asterisk appeared briefly before the target line’s onset. The benefit in response latency from this temporal cue served as an index for the alerting function. Sometimes, the star appeared exactly at the same spatial position of the target arrow. The benefit from this spatial cue served as an index for the orienting network. For the assessment of executive control, the four lines flanking the target line appeared with arrowheads as well. The arrowheads pointed either in the same (i.e., congruent) or in the opposite (i.e., incongruent)

direction of the target’s arrowhead. The reaction time difference between trials with congruent and with incongruent flankers was set as an indicator for the executive control network’s efficiency. In total, participants performed 312 trials (including 24 practice trials with feedback). The whole procedure lasted ~20 min including breaks.

Image Acquisition

From each participant, 270 T2*-weighted volumes were obtained on a Siemens Avanto 1.5T scanner (Siemens, Erlangen, Germany) at the Life & Brain Center Bonn in a single 10-min session. Participants were instructed to lie as still as possible with their eyes closed without thinking of anything in particular. Each volume consisted of 31 slices (Thickness: 3 mm, interslice gap: 0.3 mm) scanned in interleaved order parallel to the AC-PC plane (TR: 2.5 seconds, TE: 45 ms, Flip Angle: 90°, Field of View: 192 mm): Foam padding was used to constrain head movements during image acquisition.

Preprocessing

Preprocessing of the fMRI data was carried out using statistical parametric mapping (SPM8, <http://www.fil.ion.ucl.ac.uk/spm>) and the data processing assistant for resting state fMRI [DPARF, Yan and Zang, 2010] implemented in Matlab 7.8.0 (Mathworks) running on an Intel 2.53 Ghz MacBook Pro. Preprocessing contained the following steps: (1) removal of the first ten volumes, (2) slice timing to correct for within-scan acquisition time differences, (3) realignment of each volume to the session’s eleventh volume to correct for interscan movement, (4) spatial normalization to a standard echo planar imaging template, (5) spatial smoothing with a six millimeter full width at half maximum Gaussian kernel, (6) detrending to remove linear trends due to scanner drift, (7) temporal bandpass filtering (0.01 – 0.08 Hz) to remove noise from cardio-respiratory activity and scanner noise and (8) regressing out of the six motion parameters, whole-brain and white matter signals. The use of global signal regression has been questioned because it introduces spurious anti-correlations to resting state data [Murphy et al., 2009]. However, it has been demonstrated that global signal regression eliminates non-neural noise in resting state data and increases the specificity of functional connectivity analyses when positive correlations are investigated [Fox et al., 2009; Weissenbacher et al., 2009]. Because our study focuses on positive correlations within one network and not on negative correlations between networks, we chose to include global signal regression as preprocessing step.

Graph and Functional Connectivity Analysis

The functional connectivity analysis was conducted by a multiple region of interest approach as in Liu et al. [2010].

TABLE I. MNI coordinates of the sixteen nodes in the FPAN. Please view the caption of figure 1 for details on the acronyms

Brain region	<i>x</i>	<i>y</i>	<i>z</i>
Left IPS	-23	-70	46
Right IPS	25	-62	53
Left IPL	-42	-48	51
Right IPL	48	-41	54
Left vIPS	-26	-84	24
Right vIPS	35	-85	27
Left FEF	-24	-15	66
Right FEF	28	-10	58
IPCL	-55	-2	38
SMA	-2	-2	55
Left DLPFC	-40	39	30
Right DLPFC	38	41	26
Left vOC	-47	-71	-8
Right vOC	55	64	-13
Left aIns	-45	35	9
Right aIns	45	3	15

Sixteen regions of interest (ROIs) delineating the FPAN were obtained from the literature and converted to MNI coordinates [Fox et al., 2005; Toro et al., 2008]. ROIs were defined as spheres with a 6mm radius around these MNI coordinates (see Table I and Fig. 1). With a 6mm radius, each ROI comprised 904.77 mm³ or – with other words – 33 3mm³ voxels. For the graph analysis, these sixteen ROIs were set as nodes. The BOLD time series was extracted from each of the 33 voxels in each ROI and then averaged across all voxels in this ROI. Then, the functional connectivity between each pair of ROIs was computed by means of a Pearson correlation. The correlation coefficients in the resulting 16 × 16 matrix were then z-standardized by Fisher's r-to-z transformation to approximate a Gaussian distribution. This matrix represents the strength of the functional connectivity between all 16 areas in the FPAN and served as adjacency matrix for the graph analysis. Given the controversy whether there are one or two FPANs, we assessed anterior-posterior and contra-hemispheric connectivities between the ROIs to test if it was justified to treat all 16 ROIs as part of a unitary network spanning both hemispheres. For this purpose we assigned the ROIs to four different sets: right and left anterior (DLPFC, FEF and aIns) and right and left posterior nodes (IPS, vIPS, IPL and vOC). We computed the mean anterior-posterior connectivity based on the mean of the pairwise z-standardized correlations between the anterior and posterior ROIs (separately for each hemisphere and then collapsed into a single value) for every participant. The mean contralateral connectivity was calculated as the mean of the pairwise z-standardized correlations between the left and right ROIs (separately for anterior and posterior sites and then collapsed into a single value). Assessment of statistical significance of anterior-posterior and left-right connectivities was performed by two one-sample

t-tests (one-tailed against zero). Furthermore, we computed a whole-brain functional connectivity analysis between a seed region in the left IPS (6mm sphere centering around -23, -70, 46, MNI coordinate taken from Toro et al., 2008]. We then modeled the network as an undirected weighted graph $G=(V,E)$ with V representing the regions in the FPAN (see Table I) and E the z-valued connectivity strength between any two of these regions. Edges were thresholded with $k \geq 0$, i.e. negative correlations were set to zero. Thresholding is regularly applied in the context of graph theoretical approaches to functional imaging, mainly because the calculation of the centrality measures requires entries of the same sign to result in meaningful measures. Then, we computed three centrality measures: The degree centrality of node i was calculated as the sum of its connecting edges. Eigenvector centrality EC of node i was computed as the i -th entry of an eigenvector corresponding to the largest eigenvalue of the graph's adjacency matrix. Betweenness centrality BC of node i was computed as the sum of the fraction of shortest paths between any two nodes passing through it. Computation of BC was performed with the Matlab Boost Graph Library (<http://dfleisch.github.com/matlab-bgl>).

Statistical Analysis

The hypothesized relationship between the FPAN and the three attentional variables was assessed by three step-wise multiple regression procedures. Behavioral task performance in either domain (alerting, orienting, executive control) served as criterion and was regressed onto the

Figure 1.

Anatomical position of the sixteen regions of interest delineating the fronto-parietal attention network. (IPS, intraparietal sulcus; IPL, inferior parietal lobule; FEF, frontal eye field; iPCS, inferior precentral sulcus; SMA, supplementary motor area; DLPFC, dorsolateral prefrontal cortex; vOC, ventral occipital lobe; aIns, anterior insula). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

TABLE II. Descriptive Statistics (Means and Standard Errors) and Correlation Coefficients Between the ANT Indices

Index	Mean	SEM	Alerting	Orienting	Executive control
Alerting	53.71	5.72	1	-0.043	0.055
Orienting	29.14	3.14		1	-0.022
Executive Control	68.69	4.31			1

None of the correlations were significant at $P > 0.05$ (uncorrected).

centrality measures describing the FPAN ($3 \times 16 = 48$ regressors): On each step of the regression procedure, a variable was added to the model if the p -value of its corresponding F -test fell short of $P < 0.05$, and a variable was removed if the P -value surpassed a probability of $P > 0.1$. This method ensures that there are no statistically redundant predictors in the final model. The variance inflation factor and tolerance metric for none of the predictors indicated collinearity (all VIFs < 2.291 and all tolerances $> .436$). The resulting P -values of the regression procedures' F -tests that explained the most variance in the criterion were Bonferroni-adjusted to control for multiple testing.

RESULTS

Behavioral Results

Table II shows the means, standard errors, and intercorrelations for the three attentional network scores from the ANT (alerting, orienting, and executive control). All three reaction time indices were not intercorrelated which is the common finding with this version of the ANT [Fan et al, 2009]. Thus, independence of the attentional functions can be assumed for the present data set.

Functional Connectivity and Graph Analysis

To determine if the FPAN could be meaningfully reconstructed in our data set, we first computed a whole-brain functional connectivity analysis with a seed region in the left IPS. The resulting network spanned posterior and anterior sites bilaterally (see Fig. 2): In a second step we confirmed that both anterior-posterior and contralateral connectivities within the FPAN (see methods for details) differed from zero ($t(22) = 14.55$, $P < .001$ for contralateral and $t(22) = 7.33$, $P < 0.001$ for anterior-posterior connections). On the basis of these data we treated the FPAN as a unified bilateral network for the graph analysis. Table III gives an overview over the centrality measures and the mean adjacency matrix of the graph modeling the FPAN across participants. The graph analysis confirmed that all analyzed brain regions form a network spanning frontal

and parietal sites. All nodes differed significantly from zero, no matter what centrality measure was analyzed (all $P < 0.05$, FDR-corrected).

Node Centrality and Attention

Table IV sums up the results from the step-wise regression analyses. The regression of the alerting score revealed that the betweenness centrality of the right intraparietal lobule and the right intraparietal sulcus accounted for 48.6% (adjusted $R^2 = 0.486$) of the variance in the attention variable. Both nodes' betweenness showed a negative correlation with alerting, i.e., the less central the nodes in the right parietal lobule/sulcus the better attentional task performance. Figure 2 (top panels) depicts scatterplots illustrating this relationship.

The regression of the executive control score revealed a model consisting of the degree centrality of the right ventral intraparietal sulcus and the betweenness centrality of the supplementary motor area that explained 28.7% of the

Figure 2.

Whole-brain functional connectivity analysis. The FPAN was reconstructed using a seed in the left intraparietal sulcus. The z -standardized correlation map was thresholded at $P < 0.001$ (uncorr.), extend threshold $k > 10$. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

TABLE III. Mean Adjacency Matrix Modeling the FPAN and Mean Centrality Measures

	l-IPS	r-IPS	l-IPL	r-IPL	l-vIPS	r-vIPS	l-FEF	r-FEF	l-iPCS	SMA	l-PFC	r-PFC	l-vOC	r-vOC	l-Ins	r-Ins
l-IPS	1.000	0.269	0.451	0.180	0.253	0.190	0.082	0.114	0.071	0.050	0.138	0.110	0.253	0.182	0.056	0.056
r-IPS		1.000	0.202	0.264	0.223	0.147	0.138	0.174	0.110	0.096	0.105	0.148	0.287	0.222	0.069	0.063
l-IPL			1.000	0.406	0.126	0.078	0.111	0.095	0.146	0.048	0.295	0.232	0.225	0.192	0.091	0.080
r-IPL				1.000	0.094	0.053	0.129	0.211	0.154	0.120	0.221	0.276	0.233	0.223	0.082	0.121
l-vIPS					1.000	0.403	0.070	0.095	0.057	0.018	0.050	0.034	0.259	0.158	0.041	0.044
r-vIPS						1.000	0.019	0.104	0.036	0.030	0.095	0.062	0.181	0.180	0.030	0.024
l-FEF							1.000	0.228	0.138	0.157	0.046	0.039	0.114	0.096	0.083	0.074
r-FEF								1.000	0.109	0.175	0.107	0.105	0.191	0.139	0.071	0.095
l-iPCS									1.000	0.154	0.058	0.064	0.100	0.070	0.103	0.120
SMA										1.000	0.168	0.118	0.094	0.067	0.216	0.114
l-PFC											1.000	0.350	0.154	0.120	0.177	0.085
r-PFC												1.000	0.067	0.083	0.115	0.051
l-vOC													1.000	0.425	0.117	0.083
r-vOC														1.000	0.061	0.083
l-Ins															1.000	0.135
r-Ins																1.000
DC	3.332	4.013	3.535	3.497	2.701	2.668	2.327	2.870	2.253	2.634	3.198	3.039	3.440	3.378	2.322	2.113
EC	0.301	0.361	0.303	0.296	0.204	0.200	0.129	0.187	0.121	0.142	0.250	0.232	0.295	0.291	0.124	0.108
BC	23.304	18.957	14.78	14.261	23.217	15.913	22.000	23.565	20.522	17.391	20.609	15.478	19.913	16.783	26.957	35.391

DC, degree centrality; EC, eigenvector centrality; BC, betweenness centrality, for details on the other acronyms, please see Figure 1.

variance in the attention variable. Given that the executive control score of the ANT reflects reaction time increases in situations that require control, a smaller score indicates better performance in this domain. The degree centrality of the right ventral intraparietal sulcus showed a negative relationship with executive control, i.e., the higher the

TABLE IV. Results From the Step-Wise Multiple Regression of Alerting, Orienting, and Executive Control on the Three Centrality Measures Within the FPAN

Criterion	Predictor	R^2	Adjusted R^2	p	β
Alerting	Betweenness right IPL	0.533	0.486	<0.001	−0.635***
	Betweenness right IPS				−0.328*
Orienting	(Degree left ventral IPS)	(0.207)	(0.169)	(0.029)	(−0.455*)
Executive Control		0.352	0.287	0.013	
	Degree right ventral IPS				−0.410*
	SMA				0.395*

Statistics in parentheses did not hold for multiple comparison correction ($P = 0.05/3 = 0.0167$).

TABLE V. Correlations Between Connections in the Network and the Attention Variables

	r	P
Alerting Connection		
Left intraparietal sulcus - left inferior parietal lobule	0.462	0.043
Left intraparietal sulcus - left frontal eye field	−0.444	0.034
Right intraparietal sulcus - right inferior parietal lobule	0.473	0.023
Orienting Connection		
Right intraparietal sulcus - right anterior insula	0.476	0.022
Left inferior parietal lobule - right ventral occipital cortex	0.511	0.013
Supplementary motor area - right inferior parietal lobule	0.557	0.006
Left ventral intraparietal sulcus - left inferior precentral sulcus	0.501	0.012
Left ventral intraparietal sulcus - right ventral occipital cortex	−0.445	0.033
Left ventral intraparietal sulcus - right anterior insula	0.434	0.038
Left inferior precentral sulcus - right anterior insula	−0.555	0.006
Executive control Connection		
Right ventral intraparietal sulcus - left frontal eye field	−0.487	0.011
Right ventral occipital cortex - right anterior insula	0.422	0.045

Please note that the correlations do not hold for multiple comparison correction.

Figure 3.

Scatterplots depicting the relationship of the significant predictors with the alerting (top panel) and executive control (bottom panel). The attentional performance indices (RT differences between task conditions, see methods) are plotted on the y-axis. (*residuals after controlling for the influence of the first significant predictor).

local embeddement of the node in the FPAN the better the executive control performance. For the supplementary motor area, a positive relationship was observed. As for the alerting network, a higher global connectivity appears to be disadvantageous for attention. Figure 3 (bottom panel) illustrates the relationship between the centrality measures and executive control. The regression of the orienting score did not produce a finding that held the correction for multiple testing.

Links and Attention

In a next step, we tested whether single connections within the network were correlated with any of the three attention variables. There were no correlations that survived the correction for multiple comparisons (FDR-corrected). For the reader's convenience, however, Table V lists correlations that were significant at $P < 0.05$ (uncorrected).

DISCUSSION

The present study sought to assess the hypothesized link between attention paying ability and the frontoparietal attention network (FPAN) in the resting state. This was accomplished by applying graph theory to resting state functional connectivity data from multiple regions of interest and relating the resulting centrality measures of the FPAN to behavioral proxies of attentional capabilities in three different domains as provided by the attentional network test (ANT).

We found significant associations between the centrality of the right intraparietal sulcus and the right inferior parietal lobule on the one side and the alerting measure from the ANT on the other. Participants who were good at alerting showed a decreased centrality of the two intraparietal regions of interest within the network. The association was found with the betweenness centrality measure which reflects to what degree a node resides on the

shortest path between pairs of nodes within the network. Thus, BC captures information of how well a given node is globally embedded into the network or, more specifically, how much of a hub region the given node is for a global network's architecture. This global integration seems to be a decisive variable for alerting because no association was detected between the degree centrality and single links which both capture local connectivity within the network.

Furthermore, we found significant associations of the centrality of the right ventral intraparietal sulcus and the centrality of the supplementary motor area with the efficiency of the executive control system. The local connectivity of the ventral intraparietal sulcus (i.e., the degree centrality which reflects the number and strength of local connections) was beneficial for executive control, while the global embeddement of the supplementary motor area (i.e., the betweenness centrality) was inversely correlated with performance. The results on the relationship between executive control and the BC measure pointed in a similar direction as the results on alerting and BC discussed above: The higher the BC of the SMA in the network—or with other words the more likely the SMA resides on shortest paths in the network—the poorer was the participants' performance in the control domain.

No robust correlation (i.e., that holds for multiple comparison correction) was found between the FPAN and the orienting index. This nonfinding in the orienting domain is not surprising given the associations in the other two domains. Even though the three attentional domains are theoretically and empirically independent from each other, subtle overlapping in the topology of activation has been demonstrated for the alerting and executive control but not for the orienting network in a task-based activation study with the ANT [Fan et al, 2005]. Taken together, the present results are in line with the initial hypothesis that the FPAN achieves a ready state to support externally oriented cognition: Properties of the FPAN covary with an individual's attentional capability to (a) attain a state of heightened vigilance that enables the timely response to stimuli in the environment and (b) to direct attention away from distracting information toward relevant targets.

Right-hemispheric parietal association cortices alongside the intraparietal sulcus and extending into the inferior parietal lobule are implicated in sustained attention in preparation of upcoming stimuli [Corbetta et al, 1998; Corbetta and Shulman, 2002; Pardo et al., 1991]. The lateralization of attentional functions to the right hemisphere—as reported in this study—is further supported by neuropsychological evidence that hemispatial neglects are more likely to occur after lesions to the right parietal cortex. A neuroimaging study with the ANT, however, has reported no right- but left-hemispheric activation for a contrast that aimed at the isolation of alerting-related activity [Fan et al, 2005]. This difference in lateralization of neural correlates of alerting might be surprising but does not necessarily imply that the results by Fan et al. [2005] and the present

study are at odds. It might be the case that the right intraparietal sulcus and intraparietal lobule do not appear on statistical parametric maps that reflect activation differences between task conditions, but that they contribute to areas activated during alerting in terms of psychophysiological interactions [Friston et al., 1997]. In general, lateralization of the FPAN is an issue that warrants further investigations. The whole-brain functional connectivity analysis in the present study has shown both anterior-posterior and contralateral connections suggesting a unitary FPAN spanning both hemispheres. This evidence was complemented by correlation analyses between the ROIs chosen from the literature. The finding of a unitary network is in line with previous studies [e.g., Fox et al., 2005; Toro et al, 2008] but there are also other studies that report separate FPANs constrained to each hemisphere. While the present study's approach to model the FPAN as one network is valid given the connectivity patterns in the data, we cannot conclusively resolve the issue of one versus two FPANs. Future studies should address this issue by systematically varying analysis methods to precisely delineate conditions in which one or two networks show up in the data.

Similar to the results in the alerting domain discussed above, the results in the domain of executive control in the present study may look at odds with the results by Fan et al. [2005] given that neither the supplementary motor area nor the ventral intraparietal sulcus light up on statistical parametric maps contrasting incongruent and congruent trials of the ANT [Fan et al., 2005]. One of the main activated clusters for this contrast, however, is located in the anterior cingulate cortex. A recent study on resting state connectivity and executive control in children has demonstrated that weaker executive control performance covaries with stronger connectivities between the SMA and the anterior cingulate at rest, an effect additionally augmented in children diagnosed with attention-deficit/hyperactivity disorder [Mennes et al., 2011]. This finding highlights the important role of the SMA's connectivity for the domain of executive control and supports the relationship observed in this study.

A point warranting further discussion is the inverse relationship between the global connectivity measure betweenness centrality and the attentional task performance. Apparently, the more information in the network is funneled through certain nodes in the network at rest the more detrimental is the performance in an associated cognitive domain. Usually, it seems intuitive to associate stronger connectivity with an increase in functionality. This, however, was only the case for the local connectivity as reflected by degree centrality which showed up as a significant contributor to executive control performance. For all other findings, a more distributed processing at a large scale seems to be beneficial for performance. To resolve this issue conclusively, future studies should assess effective connectivity during task performance in the ANT directly and relate this to functional connectivity at rest. Future studies may also want to pursue a more balanced gender distribution, as the majority of participants in this study was female. However,

we are not aware of any gender differences in ANT performance or resting state functional connectivity. Thus, it seems unlikely that the imbalance of male and female affected our results.

Research on the functional relevance of ICN is a prosper field in neuroscience. Besides from the FPAN, at least two other ICN are of special interest for cognitive processes: First, the default mode network [DMN; Raichle et al., 2001] which consists of frontal, parietal, temporal, cingulate, and cerebellar sites. And second, the fronto-parietal control network [FPCN; Seeley et al., 2007; Vincent et al., 2008] which encompasses lateral prefrontal cortex, the anterior cingulate, the caudate head, lateral cerebellum and inferior parietal lobules. Brain regions involved in the DMN are routinely deactivated during task performance [Hampson et al., 2006; Raichle et al., 2001; Shulman et al., 1997] while the FPAN nodes show an increase in activation, especially during tasks that place demands on working memory and attention [Cabeza and Nyborg, 2000; Corbetta and Shulman, 2002; Fan et al., 2005]. This activation pattern during task conditions has inspired the terms “task-negative” and “task-positive” network for the DMN and FPAN respectively. This antagonism between the two networks is also apparent in the resting state: While the BOLD time series within the two networks are positively correlated, the correlations between the time series of both networks are negative [Fox et al., 2005, 2009; Fransson et al., 2005]. From a functional point of view it has been hypothesized that this inverse relationship reflects the opposing role of the two networks in cognition [Fransson, 2005; Vincent et al., 2008]. The DMN is thought to support internally oriented cognition, including self-referential thought and mentalization about the past and future. The FPAN, in contrast, guides externally oriented attention such as search and detection of relevant stimuli. The alleged role of the DMN in cognition has been demonstrated in experimental designs studying experimental manipulations on resting state connectivity [Andrews-Hannah et al., 2000; Fransson, 2005] and by means of individual difference designs [e.g., Liemberg et al., 2012; Sheng et al., 2010]. For the FPAN, however, such evidence was scarce. This study fills this gap in the literature and provides empirical evidence that the FPAN plays indeed an important role in the cognitive domain of attention. By confirming this, the present finding is also in line with assumed functional antagonism of the DMN and FPAN in cognition. The third “cognitive” ICN, the FPCN, is thought to integrate information from both networks to guide goal-directed behavior because the brain regions organized in the FPCN play pivotal roles in working memory [Curtis and D’Esposito, 2003] and executive control [Ridderinkhof et al., 2004]. Within parietal cortices the FPCN is anatomically located between the DMN and FPAN which suggests its integrative role in information processing. Direct evidence for the FPCN’s implication in cognition stems from an individual differences analysis [Seeley et al., 2007]. In this study, the connectivity between a cluster in the right

intraparietal sulcus and the overall network at rest was shown to covary with executive control performance: Higher connectivity reflected better performance in the trail-making test. Even though these data relate to a different ICN, the connectivity pattern mirrors the present study’s result, as local connectivity of a parietal region corresponds to better executive control performance (see the association between the degree centrality measure of the right ventral intraparietal sulcus and executive control in the present study). Apparently, both fronto-parietal networks (the FPAN and the FPCN) play a role in executive functioning. Future studies should consider the assessment of the relative contribution and joint interplay of either network on this behavioral phenotype. Besides the study of single ICN it will become imperative to study the global integration of different ICNs and its impact on intellectual performance. For example, a pioneering study by van den Heuvel et al. [2009] has demonstrated that global communication efficiency on the whole-brain level at rest is related to general intelligence. Given that general intelligence is related to working memory and executive control performance it would be interesting to see how the organization of connectivity within and across networks relates to these cognitive phenotypes.

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