

**Individual Differences in Resting-state Functional MRI are Relevant
to the Unity and Diversity of Executive Function**

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Abstract

Resting-state functional MRI (rs-fMRI) is thought to reflect the intrinsic functional organization of the brain. Studies of group differences in measures of rs-MRI are pervasive throughout the field of cognitive neuroscience and clinical neuropsychology, but the relationship between the resting state of the brain and individual differences in performance on psychological tasks in a normal population remains poorly understood. Moreover, the limited available research fails to adequately relate individual differences in the resting brain to theoretically motivated constructs that are thought to relate to underlying processes responsible for humans' ability to regulate thoughts and actions (i.e. – executive functions). Ninety-one college-aged participants completed a six-minute resting state fMRI scan and a battery of tasks measuring important aspects of executive function (see Miyake & Friedman, 2012): inhibition of a prepotent response (antisaccade task), task set shifting (category switching task), and working memory updating (keep-track task). Using Independent Components Analysis (ICA), we identified several networks of regions (Intrinsic Connectivity Networks, ICNs) with temporally correlated time courses. We found that 1. individuals who activated subsystems of the default network to a greater degree had higher common executive function and working memory updating and 2. individuals who activated right and left frontoparietal control network to a greater degree had higher task set shifting and working memory updating, respectively. Additional predictors of working memory updating were the degree to which individuals' left frontoparietal control ICN was negatively correlated with a subset of regions from the default mode ICN and also the degree to which individuals' right frontoparietal control ICN was positively correlated with a different subset of regions from the default mode ICN.

Finally, we employed a recent methodology (Dual Regression) to explore areas associated with an ICN that covary with individual differences in executive function. Dual regression revealed that covariance of four regions along with ICNs predicted EF: increased presence of right anterior prefrontal cortex in the dmPFC subsystem of the default network predicted higher common EF, increased presence of left lateral parietal region in the right frontoparietal control network predicted higher task set shifting, and increased presence of left middle frontal gyrus and postero-medial prefrontal cortex in the left frontoparietal control network predicted higher working memory updating. The results of the current study have important implications for our understanding of executive function processes and individual differences in the brain at rest. In particular, we discuss how underlying brain processes responsible for executive function performance likely sculpt the intrinsic functional organization of the brain over time and to a different degree based on skill.

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Individual Differences in Resting-state Functional MRI are Relevant to the Unity and Diversity of Executive Function

When individuals are not engaged in a directed task (“resting state”), large networks of brain regions share similar temporal patterns of low frequency BOLD response (as measured by resting state functional MRI, rs-fMRI). A dominant theme in the literature is that patterns observed in rs-fMRI represent the intrinsic functional organization of the brain (Fox & Raichle, 2007). That is, regions of the brain that exhibit similar temporal patterns during the resting state do so because those regions have coactivated together in the past (Wig, Schlaggar, & Petersen, 2011). Networks of regions that activate together during the resting state (referred to as intrinsic connectivity network, ICNs) bear strong resemblance to patterns of activation observed during performance of certain classes of task or operation (e.g. - frontoparietal control network composed of regions typically implicated in fMRI studies of executive function; Yeo et al., 2011). The current study address the question of whether or not individual differences in measures of rs-fMRI within ICNs thought to be behaviorally relevant (based on studies of task-induced activations) are predictive of behavior outside the scanner. Specifically, do measures that quantify resting-state activity within a given ICN predict individual differences in executive function ability?

Several studies have shown rs-fMRI measures are stable across time within individuals and furthermore that individuals differ in the degree to which they activate particular networks (Shehzad et al., 2009; Guo et al., 2012). Additionally, differences in ICN expression, such as increased or decreased activity of a particular ICN, have been observed in a plethora of clinical populations when compared to control participants (e.g. – mild cognitive impairment (Greicius et al., 2004), Alzheimer’s disease (ibid.), panic disorders (Pannekoek et al., 2012), depression (Zhu et al., 2011; Greicius et al., 2007), amongst others). In addition to their clear implication in differentiating clinical populations from controls,

individual differences in rs-fMRI has been linked to trait differences in a number of behavioral measures including fluid intelligence (Cole et al., 2012), attentional control in the face of distracting information (Kelly et al., 2008), and working memory ability (Hampson et al., 2006; Gordon et al., 2012). The current study intends to further explore the relationship between individual differences in a neurologically-normal population in activity of the resting brain and individual differences in behavioral indices of the ability to direct thoughts and actions in a goal-directed manner, referred to as executive function.

Behavioral Relevance of rs-fMRI

Individual differences in rs-fMRI have been quantified with a variety of methodological techniques (e.g. – independent components analysis, ROI-to-ROI functional connectivity, clustering, graph theoretic techniques) (Beckmann, 2012; Yeo et al., 2011; Wang, Zuo, & He, 2010). These methods differ along two dimensions: 1. the size of the functional unit of study, varying from broad (networks of brain regions) to narrow (individual brain regions) and 2. whether the networks/regions-of-interest are determined *a priori* or via data driven methods. What follows is a review of previous studies that have found a significant relationship between individual differences in rs-fMRI measures and a variety of behavioral measures. Here we focus on previous work that is related to individual differences in executive function and related processes.

Some studies have investigated whether or not the strength of correlation between two given ICNs is predictive of behavior. ICNs in these studies are defined using either Independent Components Analysis (ICA), a data driven approach that decomposes functional brain data into a set of statistically independent spatiotemporal components (as in Kelly et al., 2008) or an approach in which networks are identified as those voxels across the whole brain whose activation significantly correlates with an *a priori* region of interest (as in Thompson et al., 2012). The ICNs being investigated in these studies are named based on their activation during psychological processes (i.e., not during rest). For example the “task-positive” network is composed of frontal and parietal regions typically implicated in cognitive

control tasks. The “task-negative” network is composed of ventro-medial prefrontal cortex, posterior cingulate cortex, precuneus, anterior temporal cortex, and lateral parietal cortices, regions which typically deactivate during executive function tasks. A stronger negative correlation between time courses for each participant’s task-positive and task-negative ICNs is associated with less variable performance during a flanker task (Kelly et al., 2008) and faster response times on a vigilance task (Thompson et al., 2012). The flanker task is an executive function task requiring top-down control in the face of distracting information while vigilance tasks are considered part of a different family of attention tasks that primarily measure sustained alertness (Petersen & Posner, 2012). Based on differences in the task used in these two studies, it is unclear which aspects of attention are related to the intrinsic relationship between the task-positive and task-negative ICNs.

Other studies have examined whether or not the strength of correlation between individual regions of the brain is predictive of behavior. Seed-selection, or the process of determining which specific regions are of interest, varies from study to study. Some research has been interested in the relationship among regions within the same ICN as a predictor of behavior. For example, greater correlated activity amongst default network regions such as posterior cingulate cortex (PCC), medial frontal gyrus (MFG) and ventral anterior cingulate cortex (vACC) predicts higher performance on a verbal working memory task (Hampson et al., 2006). Similar research has found that increased functional connectivity between a lateral parietal ROI and the rest of an ICA-identified executive-control network predicts performance on a neuropsychological test of executive functioning, the trail-making test (Seeley et al., 2007). These studies suggest that variability in working memory and trail making is partially explained by connectivity within the executive control network or by its connectivity with other systems.

Another method for exploring either network-to-network or ROI-to-ROI relationships as a predictor of behavior is through graph theoretic measures. Graph theory (see Bullmore & Bassett, 2011;

Bullmore & Sporns, 2009 for reviews) defines the brain as a set of nodes and edges, forming a graph. Nodes in graphs are either anatomical regions, regions of interest from a task-based or many task-based studies, or regions from a data-driven parcellation of resting state activity (e.g. – clustering analysis). Edges are a measure of the functional relationship between nodes. Often times the functional measure represented by edges is a time course correlation between two nodes. Graph theory measures are usually summary measures of any given node's or network of node's (sometimes called a neighborhood) relationship to other nodes or neighborhoods. One behaviorally relevant graph theoretic measure is global connectivity, which is a summary measure of the average time course correlation between each ROI and every other voxel in the brain. Greater global connectivity of lateral prefrontal cortex is associated with higher fluid intelligence and working memory capacity (Cole et al., 2012). Another measure, modularity, indexes the efficiency of local processing within a network of nodes. Higher modularity within a cognitive control network has been linked to greater working memory capacity (Stevens et al., 2012). Similar to other methods, graph theoretic measures suggest that variance in executive function can be partially explained by individual differences in measures of the intrinsic dynamics of cognitive control regions.

In summary, a wide range of behaviors have been linked to individual differences in a number of brain regions and networks of brain regions. Some themes do emerge, notably in the form of multiple links between behavior and resting state activity in default network, a variety of different task positive or control networks, and individual regions that are typically contributors to these networks (e.g. – cingulate cortex, lateral frontal cortex, temporoparietal areas). However, one limitation of these studies is the lack of a theoretical context to place the link between individual differences in rs-fMRI to aspects of the EF tasks thought to contribute to the intrinsic organization of the brain. That is, how does the pattern of relationships highlighted above relate to psychological theories of executive function? For example, individual differences in performance on both the flanker task and a vigilance task have been

linked to resting state activity in the same networks of brain regions. There is some degree of overlap with regard to psychological processes involved in performance of vigilance and flanker tasks, so it is necessary to more thoroughly tease apart which processes or subprocesses contribute to the intrinsic organization of the brain, as assessed through rs-fMRI.

Executive Function

Given the many previously identified relationships between behavior and rs-fMRI, a theoretical model is necessary to better understand behaviorally-relevant resting state activations in terms of the underlying mechanisms that contribute to intrinsic dynamics and also with regard to individual variability in these mechanisms. Thus, the current study attempts to address the question “Can a theoretical model of executive function clarify the link between the individual differences in intrinsic functional organization of the brain and variability in measures that index brain mechanisms implicated in executive function ability?” Considerable progress has been made toward developing a theoretical model of executive function (for a review, see Miyake & Friedman, 2012). Miyake and Friedman suggest that many important aspects of executive function can be best typified through latent constructs that capture not only common underlying ability required to perform well on executive tasks (the unity of executive function; i.e., – the ability to actively maintain goals) but also process-specific abilities (the diversity of executive function; i.e., – the ability to flexibly switch between task set, the ability to update working memory). The resulting model of executive function was derived from an analysis of nine tasks designed to measure three categories of executive function: inhibition, shifting, and working memory updating. A latent factor analysis of performance on those three categories of executive function tasks revealed that variance in performance across individuals could be explained entirely by three factors. Rather than three factors reflecting their three *a priori* categories of tasks, a different pattern was observed. The first factor loaded approximately equally on all tasks and is thought to represent ability that is shared between all of the executive function tasks chosen for the battery (termed common

executive function, Common EF). Common EF is thought to represent the general ability to maintain a goal. The second factor loaded heavily on tasks that required flexibly shifting between different task/mental sets (termed shifting-specific executive function or set shifting). The third factor loaded heavily on tasks that necessitated rapidly adding to or deleting from the contents of working memory (termed updating-specific executive function or working memory updating).

The Unity and Diversity model suggests that variability in executive function ability across individuals may be partially explained by underlying differences in the brain processes that subserve those executive functions, such as the maintenance of representations in prefrontal cortex or the mechanisms involved in shifting between representations of task set (Chatham et al., 2011; Herd, Banich, & O'Reilly, 2006). Additionally, nearly a decade of neuroimaging work has converged on the localization of brain processes involved in executive function, such as higher-level sources (e.g. - frontal cortex) or lower-level sources (e.g. - parietal cortex) of executive control. Do individual differences in executive function ability manifest in measures of rs-fMRI that are thought to measure the degree to which regions of the brain share a common history of coactivation? And more importantly, do these behavioral measures relate to individual differences within specific ICNs that have previously been related to different aspects of executive function (e.g. – does working memory ability relate specifically to ICNs composed of regions linked to working memory ability)?

Models of executive function can help clarify predictions. In the context of the Unity and Diversity model of executive function, maintenance of goals and task sets is related to the common EF. The dual network model of top-down control focuses on the distinction between brain systems responsible for maintenance of task goals versus moment-to-moment control over the instantiation of those goals (Dosenbach et al., 2008). According to this model, the cingulo-opercular network, which is composed of frontopolar and cingulate regions, is responsible for maintaining abstract notions of goals and task sets that are necessary for performing all kinds of tasks in everyday life and in the

laboratory. One prediction, therefore, might be that there should be a relationship between resting state brain activity in frontopolar and cingulate regions and performance on measures of EF that are thought to index maintenance of goals. In addition to the maintenance of goals, performance in real life and on executive function tasks also depends on our moment-to-moment ability to fluidly switch between these representations of goals and task sets. The dual network model has attributed these moment-to-moment functions to the frontoparietal network, which is composed of lateral frontal and parietal regions. Hence, another prediction would be of a relationship between resting state brain activity in lateral frontal and parietal regions and performance on measures of EF that are thought to index moment-to-moment control. In the context of the Unity and Diversity model, moment-to-moment control can be indexed by the diversity measures such as task set shifting and working memory updating.

To explore the relationship between rs-fMRI and executive function, we propose a three-part analysis that addresses an important limitation of prior studies that examine rs-fMRI and individual differences in performance on executive function tasks. Historically, studies have used only one level of analysis (e.g. – behavior as related to ICNs, behavior as related to ROIs) leaving open the possibility that findings may be biased by the approach employed. To overcome this limitation and provide converging evidence for our conclusions we supplemented typical ICA analysis of individual differences in the expression of certain a priori ICNs with additional analysis of individual differences in ICN-to-ICN time course correlations. Finally, we use a recent Dual Regression technique (Beckmann et al. 2009) that provides a method for exploring between-subject differences in ICNs (that can covary with behavioral differences) at the level of individual brain regions. In combination, these methods permit exploration of the relationship between executive function and rs-fMRI measures at each previously highlighted level of analysis, and within the framework of a strong theoretical model of EF which has been supported by a wealth of empirical work (Miyake & Friedman, 2012).

Material and Methods

Participants

One hundred individuals (91 analyzed, 48 females) ages 18 to 34 years ($M = 20.8$) from the University of Colorado Boulder participated for payment over two sessions. Participants were paid \$25.00 per hour for the fMRI session and \$10.00 per hour for the behavioral session. Session one involved the administration of behavioral tasks that measured executive function ability. Session two involved the acquisition of anatomical and functional brain data via magnetic resonance imaging. The two sessions occurred within an average of 31.6 days of each other. Functional brain data from six participants was discarded due to 40% or more of frames having unacceptable levels of displacement and/or intensity (as determined by the Artifact Detection Toolbox). Guidelines for acceptable frames were taken from Power et al. (2012). Additionally, data from three participants was discarded due to failure to comply with rules on one or more of the behavioral tasks. All presented results are from analyses of data from the remaining 91 participants.

Data Acquisition

In session one, three behavioral tasks were administered from the battery of tasks used in the Unity & Diversity Model of Executive Function (see Miyake et al., 2000; updated in Miyake & Friedman, 2012): antisaccade task, category switching task, keep track task.

In session two, participants were scanned in a Siemens Tim Trio 3T scanner. High resolution MP RAGE T1-weighted anatomical (acquisition parameters: repetition time (TR) = 2,530ms, echo time (TE) = 1.64, matrix size = 256 x 256 x 192, flip angle (FA) = 7 deg., slice thickness = 1mm) and T2*-weighted echo-planar functional (acquisition parameters: number of volumes = 165, TR = 2,000ms, TE = 29ms, matrix size = 64 x 64 x 33, FA = 75 deg., slice thickness = 3.5mm, field of view (FOV) = 240mm) scans

were obtained. During the resting state scan, participants were instructed to relax and close their eyes. Analysis of brain data is described below.

Paradigms and Behavioral Data Analysis

The antisaccade task (adapted from Roberts, Hager, & Heron, 1994) is an executive function task that measured a person's ability to inhibit an automatic process (an eye movement). Participants were instructed to focus on a centrally located fixation cross (lasting 1-4 sec). When the fixation cross disappeared, an initial cue flashed either to the right or left of fixation. The cue always appeared the same number of pixels to the right or left of the central fixation cross. Next, the cue disappeared and the target appeared for 150ms and then is masked with gray cross-hatching. The target and mask also appeared the same number of pixels to the left or right of the central fixation cross. The target was a digit, 1 through 9. Participants named the number they saw aloud and the experimenter typed in their response, triggering the next trial to begin. In some parts of the task, the cue was helpful in that it indicated the location at which the target appeared. That is, the cue appeared on the left of the screen and was followed by the target on the left as well (an example of a prosaccade trial). On other trials, the cue appeared on the left but the target appeared on the right (an example of an antisaccade trial). The task began with a block of prosaccade trials to establishing an automatic association between the cue and target occurring on the same side of the screen. Participants were then given three blocks of antisaccade trials in which the cue was not helpful (i.e. - does not indicate the location of the target). Participants typically vary in their ability to identify the target on antisaccade trials because it is difficult to inhibit the automatic association established early in the experiment and the desire to look towards an object presented in peripheral vision. The dependent measure was average accuracy for the three blocks of antisaccade trials. Participants with higher accuracy on these three blocks are said to have greater executive control. There were 164 total trials.

The category switching task, adapted from Mayr & Kliegl (2000), is an executive function task that measured a person's ability to quickly and accurately switch between different modes of categorization. Participants were asked to categorize words describing living/non-living things (e.g., alligator/coat) and things smaller/larger than a soccer ball (e.g., knob/lion). After pure blocks categorizing along a single dimensions (e.g. – as either living or non-living) for 32 trials each, participants completed two blocks of 64 trials each that contained a mixture of trials with judgments along the living and size dimensions. The dependent measure was the switch cost: the difference between average reaction time for correct switch trials and correct repeat trials during the mixed blocks for each subject.

The keep track task, adapted from Yntema, (1963), is an executive function task that measures a person's ability to update their working memory to conform to the demands of the task. A stream of words was presented, one at a time. The words belong to six categories: relatives, countries, colors, animals, metals, and distances, with six words in each category. Participants were asked to keep track of the most recent word presented from each of two to five categories and report their answer verbally at the end of the trial. Sixteen trials were administered, each trial containing a stream of 15-25 words. After two practice trials with two categories to remember, there were four blocks of two-, three-, four-, and five-category trials, randomly ordered within each block. Each trial began with the list of categories, which remained at the bottom of the screen until the final recall. Each word appeared for 2000ms, followed by the next word. The dependent measure was each participant's accuracy in recalling lists of varying length.

In accordance with the unity and diversity model, scores from the three executive function tasks were transformed into constructs analogous to the three latent factors derived from a larger analysis of 9 executive function tasks (Miyake & Friedman, 2012): common EF, set shifting, and working memory updating. Common EF measure reflects ability that is shared between all executive function tasks (e.g. - ability to maintain a goal). Common EF was calculated by taking the average of each subject's three tasks

converted to a Z value (across the group of 91 participants). Set shifting reflects the ability to flexibly shift between different task/mental sets and was derived by residualizing each participant's score on the category switching task (regressing out antisaccade task and keep track scores). Working memory updating reflects the ability to rapidly add to or delete from the contents of working memory and was derived by residualizing each participant's score on the keep track task (regressing out antisaccade and category switching scores). Higher scores on three composite measures correspond to greater ability in that construct (i.e. - maintain a goal, shift between task/mental sets, or update working memory).

Brain Data Overview

Analysis of brain data was performed via a three-part process. First, Independent Components Analysis (ICA) was used to identify networks of brain regions that coactivated together across the group of subjects. The main measure derived from this step is an effect size for each subject for each group level component representing the degree to which each subject activated the brain regions that make up each component. In the second step, time courses of activation were extracted for each component for each subject. These time courses were used for within-subject pairwise correlation analysis for pairs of networks to determine the temporal correlation between pairs of components within a given subject. The final step (called Dual Regression) determined differences in components between subjects that significantly covary with a behavioral measure (e.g. – a measure of executive function). While the first step identified which regions consistently coactivated together across the group of subjects, Dual Regression may identify regions that activate for some subjects but not others. Importantly, Dual Regression uses subject-specific components to determine which regions covary with a behavioral measure. Dual regression can, for example, determine that the more a subject activates a given region (whether or not it is part of the group-level component) varies in relation to his or her level of executive function.

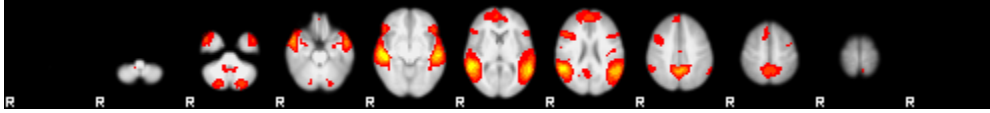
Independent Components Analysis

In order to decompose the functional brain data into various independent spatiotemporal components, Independent Components Analysis (ICA) was performed on the functional scans using Melodic ICA version 3.10 (Beckmann & Smith, 2004), part of the FSL tools (Jenkinson et al., 2012). To account for signal settling, the first four volumes of each individual functional scan were removed, yielding 161 volumes per subject for additional analysis. Input scans for Melodic were preprocessed to correct for head motion using MCFLIRT, FSL's motion correction tool. Within Melodic, brain extraction (BET) was used to remove signal associated with non-brain material (e.g. – skull, sinuses, etc.).

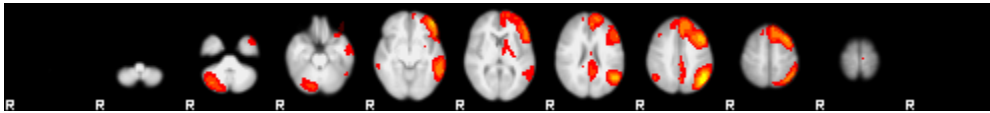
Analysis with Melodic yielded 34 group-level components. Components that were obviously explained by edge effects or movement were removed from further analyses. The remaining components were sorted based on their power distribution curve. Components with a main peak of power distribution that did not lie in the lowest frequency bin (0 Hz – .03 Hz) were discarded. This procedure yielded 18 signal components that likely reflect actual Intrinsic Connectivity Networks. We limited further analysis to those ICNs that have been previously associated with individual differences in behavioral measures of executive function at rest or during performance of the task itself ($n = 4$): dorsal medial prefrontal cortex subsystem of the default network, left frontoparietal control network, right frontoparietal control network, and the hubs of the default network. Additionally, the visual network was identified and is depicted below. The visual network was chosen as a control network.

Components-of-interest for further analyses are presented below. Component maps represent the probability of inclusion in the group level independent component and have been thresholded at $z > 2.50$. Where appropriate, components have been named based on their similarity to previously discovered networks implicated in resting-state and task-based ICA analysis of fMRI data:

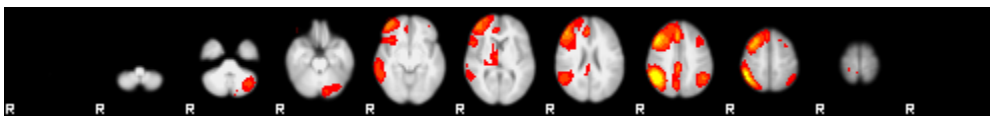
dmPFC subsystem of Default Network (dmPFC):



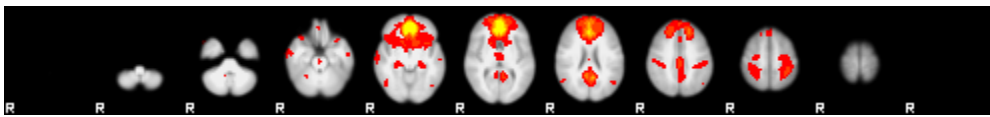
Left Frontoparietal Control (LFPCN):



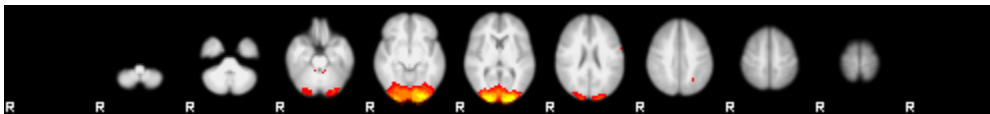
Right Frontoparietal Control (RFPCN):



Hubs of Default Network (Hubs):



Visual Network (used for control comparisons):



For each of the components of interest, subject effect sizes were extracted. These effect sizes serve as the individual difference score for the primary analysis and can be interpreted as a scaling factor for the activation of the time series of the component of interest. That is, subjects with larger effect sizes for the LFPC network have larger amplitude activations across that network during the resting state scan. For each pairwise relationship between executive function construct and ICN-of-interest, a higher-level model was run regressing executive function construct scores on subject effect sizes controlling for the grand mean activation of each component. Reported in results are significant relationships ($p < .05$) between activation of a priori ICNs of interest and one of the executive function

constructs. All reported relationships were compared to the relationship between visual network and the executive function construct of interest using the Fisher's *r*-to-*z* transformation. These comparisons were done to examine the specificity of relationships between executive function and any given network. The visual network was chosen as the control network because it was hypothesized that activity in the visual network should not be related to executive function.

In an additional step, time courses were extracted for each group level ICN for each individual. Pearson's coefficient of correlation was calculated for pairwise relationships between default network subsystems and both left and right frontoparietal control networks because, historically, the relationship between default network and control networks have been predictive of behavior (Kelly et al., 2008; Thompson et al., 2012).

Dual Regression

Dual regression is a technique for exploring higher-level differences in Intrinsic Connectivity Networks (Beckmann et al., 2009). Dual Regression is a two-step process that takes unthresholded group-level independent component maps and resting state functional brain data as input and generates both subject-specific component time courses and subject-specific spatial maps as output.

Dual regression can be broken down into two steps: First, for each subject, the group-average set of spatial maps is regressed (as spatial regressors in a multiple regression) into the subject's 4D spatio-temporal dataset (i.e. brain volumes across time). This results in a set of subject-specific time series, one per group-level component. Next, those time series are regressed (as temporal regressors, again in a multiple regression) into the same 4D dataset, resulting in a set of subject-specific components, one per group-level component. It is possible for subject-specific components to include regions that are not present in the group-level components. The resulting subject-specific components are then used to determine spatial areas that covary with behavioral covariates of interest, in our case, level of executive function. In the current analysis, subject-specific component maps for the LFPC, RFPC,

and dmPFC networks were analyzed using Randomise, FSL's permutation testing tool. The resulting image was thresholded at $p < .005$ and represent areas across the subject-level components that covary based on a behavioral covariate of interest. In the context of the current study, resulting p maps show areas of the brain that are more present in the group level component based on having higher executive function. Because the analysis uses whole brain unthresholded group-level components, areas outside the group component can also emerge as significant predictors of executive function constructs.

Results

Behavioral Data

In the current study, we will relate individual differences in executive function constructs to individual differences in rs-fMRI. Before reducing the data to a common and two specific EF constructs, we performed a checks to ensure the data was of sufficient variability for a study of individual differences and that the results were consistent with prior studies using these tasks (i.e. – task performance is, on average, below ceiling). **Figure 1** shows raw task (not yet transformed into constructs) variability for the three task used in the current study. The boxplots confirm that these tasks do vary across individuals. It should be noted that this is expected as these specific tasks were designed to elicit the greatest possible variability within the university population tested in the current study. Additional statistics of interest are: mean switch cost of 174.3ms (difference between repeat and switch trials), mean keep track accuracy of 76.1 percent, and mean accuracy of 75.5 percent on antisaccade trials of the antisaccade task. Mean performance in the current study was slightly better than performance in a much larger (n=550+) analysis of the same tasks in a group of younger adults (mean age of 17.3 compared to 20.8 in the current study; Friedman et al., 2008).

Relationship between ICA Networks and Executive Function

For each pair of executive function constructs and a priori networks of interest, a model was run regressing executive function construct scores on subject effect sizes for the ICN while controlling for the grand mean activation of each component. The subject effect size indicates the degree to which there is coactivation of regions within this network. The following are significant relationships. Following reporting of significant relationships, tests of specificity are reported. For each significant relationship between an ICN and EF construct, that relationship was compared to the relationship between the visual ICN and the same EF using Fisher's z (higher z = greater difference). Additionally, for each significant

relationship between an ICN and EF construct, that relationship was compared to the relationship between a related ICN (opposite hemisphere for lateralized ICNs, alternative ICN subsystem in the case of the default network ICNs) as an additional test of specificity.

Common executive function and dmPFC subsystem of the default network were related ($z = 2.26, p < .012$) such that individuals with larger effect sizes for the dmPFC subsystem network effect sizes had higher common EF. The relationship between dmPFC subsystem and common EF was higher than the relationship between common EF and the visual network (fisher's $z = 2.21, p_{(one-tailed)} < .013$), showing some degree of specificity, but was not greater than the relationship between common EF and the hubs of the default network (fisher's $z = 1.28, p_{(one-tailed)} = .100$), showing that Common EF may be related to the default network in general rather than the hubs subsystem specifically.

Working memory updating and LFPC network were related ($z = 2.65, p < .004$) such that individuals with larger effect sizes for the LFPC network had better updating. The relationship between LFPC and working memory updating was greater than the relationship between working memory updating and the visual network (fisher's $z = 1.81, p_{(one-tailed)} < .035$) and working memory updating and RFPC (fisher's $z = 3.31, p_{(one-tailed)} < .001$), indicating the relationship between working memory updating and LFPC ICN is both significant and specific. In addition, the working memory updating component and the hubs of the default network were related ($z = 2.24, p < .012$) such that individuals with larger effect sizes for the hubs of the default network had higher working memory updating scores. The relationship between hubs and working memory updating was marginally greater than the relationship between working memory updating and the visual network (fisher's $z = 1.51, p_{(one-tailed)} = .065$) but not greater than the relationship between working memory updating and the dmPFC subsystem (fisher's $z = 0.55, p_{(one-tailed)} = .291$), indicating the relationship between working memory updating and the hubs of the default network is significant but not specific with regard to either the control ICN or a related ICN.

Finally set shifting and the RFPC network were related ($z = 1.96$, $p < .025$) such that individuals with larger effect sizes for the RFPC network had higher shifting specific scores. The relationship between RFPC and shifting was not greater than the relationship between shifting and the visual network (fisher's $z = 1.13$, $p_{(\text{one-tailed})} = .129$) or shifting and the LFPC network (fisher's $z = 0.77$, $p_{(\text{one-tailed})} = .221$), indicating again a significant relationship that is not specific with regard to a control ICN or a related ICN. **Table 1a** summarizes these findings.

ICN-to-ICN Time Course Correlations predict Working Memory Updating

For each of the identified networks-of-interest from the group ICA analysis, a time course of activity was extracted for each participant. Within-participant Pearson correlations were calculated for each pair of network time courses. **Figure 2** shows summary statistics for sample pairs of networks. Sample pairs of networks were chosen based on hypothesized relationships that could be used as a validity check (i.e. – related networks should be positively correlated; unrelated networks should be negatively or not correlated). This figure shows that, on average, the dmPFC subsystem ICN and frontoparietal control ICN time courses were negatively correlated, the default network subsystem ICN time courses were positive correlated, and left and right frontoparietal control ICN time courses were positively correlated. Collectively, these results serve as a check that subsystems of or lateralized aspects of the same networks (default and control) are positively correlated while opposing networks are negatively correlated. A higher-level analysis was then performed correlating the network-to-network correlations with individual difference scores for each of the three executive function constructs. In the current analysis, only default to control network pairs were correlated with executive function consistent with the inverse relationship between default network and control networks that has been observed previously and which has been predictive of behavior (Kelly et al., 2008; Thompson et al., 2008).

Only working memory updating scores were predicted by correlations between network time course correlations. **Table 1b** depicts significant relationships between pairwise network time course correlations and working memory updating score. The working memory updating component was predicted by the correlation of the dmPFC subsystem and LFPC network such that individuals with more negatively correlated networks had higher working memory updating ability ($r = -.254, p < .015$). This relationship is consistent with previous studies of network-to-network relationships that found stronger negative correlations as predictive of greater executive function. The working memory updating component was also predicted by the correlation of the hubs subsystem of the default network and RFPC network such that individuals with more positively correlated networks had higher working memory updating ability ($r = .263, p < .012$). This relationship is a surprising finding due to the reversal in directionality when compared to the previous result. Hence, the time course correlation analysis revealed that the relationship between default and control networks is predictive of working memory updating, however, further exploration of the directionality of these relationships is needed.

Dual Regression

For each of the executive function constructs, a follow-up Dual Regression analysis was run on the strongest predictive network from the initial analyses of subject effect sizes: dmPFC subsystem of the Default Network ICN for common EF, LFPC ICN for working memory updating, and RFPC ICN for set shifting. **Table 1c** shows areas of activity that covary with each of the three aspects of executive function. Interpretation of these figures is such that increased presence of the highlighted region in the ICN of interest is associated with higher executive function.

In the Dual Regression analysis of dmPFC subsystem and common EF, a region in right anterior prefrontal cortex ($X = 30, Y = 54, \text{ and } Z = 12$) was identified. It should be noted that this region does not appear in the thresholded group-level dmPFC subsystem ICN, suggesting the dmPFC subsystem ICN was

composed of different regions based on common EF score. Individuals with higher common EF scores had an increased presence of this anterior prefrontal region within their dmPFC subsystem ICN.

In the Dual Regression analysis of LFPC ICN and working memory updating, two regions were identified as covarying with behavior: left middle frontal gyrus ($X = -42$ (33), $Y = 26$ (38), and $Z = 32$ (26)) and postero-medial prefrontal cortex ($X = 2$ (22), $Y = 42$ (42), and $Z = 40$ (38)). Individuals with higher working memory updating scores had an increased activation of these regions, which are part of the LFPC ICN.

In the Dual Regression analysis of RFPC ICN and set shifting, a region in left parietal cortex ($X = -56$ (36), $Y = -54$ (18), and $Z = 36$ (27)) was identified. It should be noted that this region does not appear in the thresholded group-level RFPC ICN, suggesting that the RFPC ICN was composed of different regions based on set shifting score. Individuals with higher set shifting scores had an increased presence of this left parietal region within their RFPC ICN.

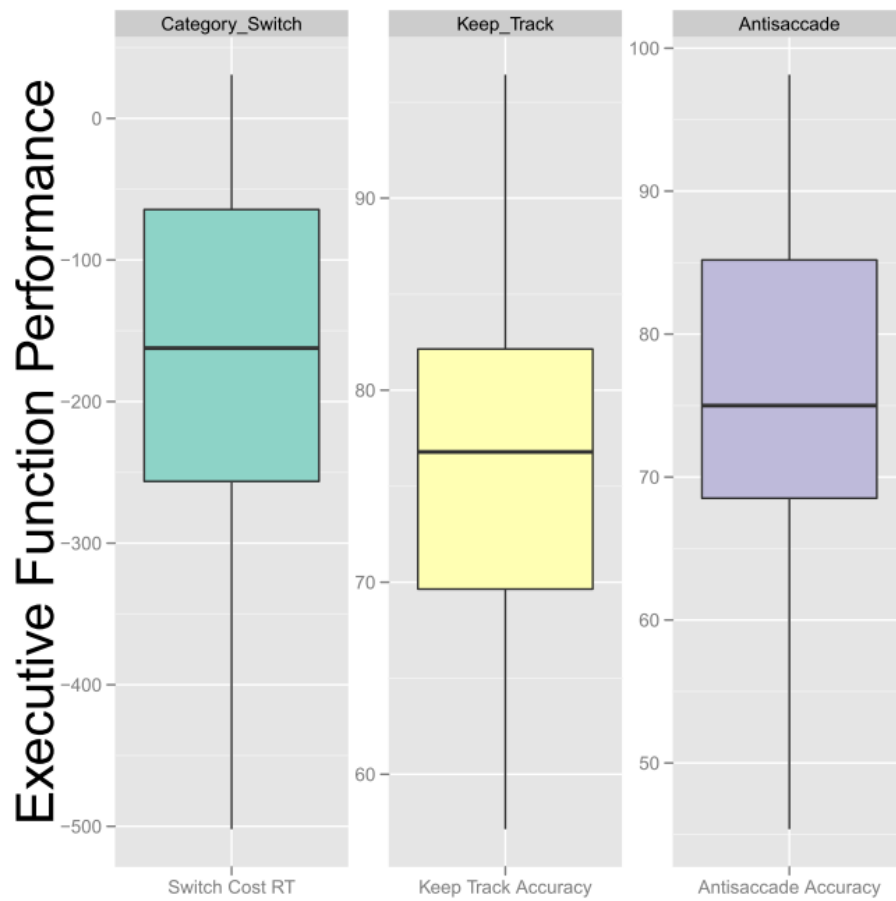
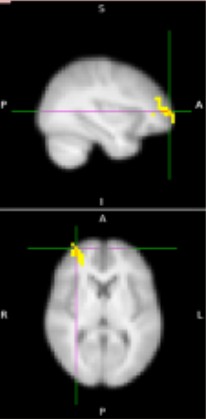
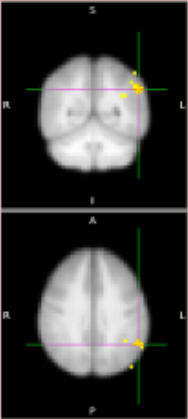
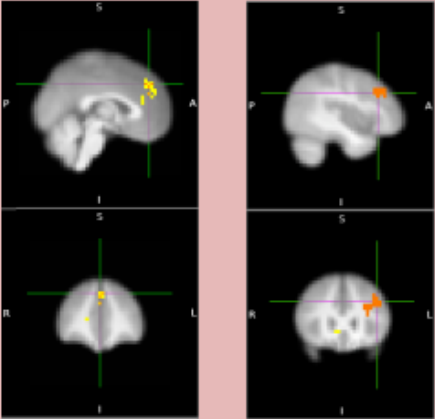
Figure 1. Group Performance on Executive Function Tasks

Figure 1 shows variability across participants for each of the three executive function tasks. Scale (either reaction time or accuracy) for each boxplot is labeled on the x-axis. Directionality is such that higher on the y-axis corresponds to greater performance on the given task.

Table 1. Results Overview

Common EF		Shifting	Updating
a.	dmPFC Subsystem	R. Frontoparietal Control	L. Frontoparietal Control Hubs Subsystem
b.	X	X	L. Frontoparietal Control – to – dmPFC Subsystem correlation R. Frontoparietal Control – to – Hubs Subsystem correlation
c.	coactivation of highlighted regions w/ dmPFC Subsystem varied with Common EF: 	coactivation of highlighted regions w/ R. Frontoparietal control varied with Shifting: 	coactivation of highlighted regions w/ L. Frontoparietal control varied with Working Memory Updating: 

1a. ICA network effect sizes: Table 1a shows the relationship between EF constructs and subject effect sizes for ICA networks. The directionality of each association is such that greater executive function is associated with a larger effect size for the noted network. Checked backgrounds represent relationships that pass threshold of significance but are not specific (are not significantly different from relationship between EF construct and other ICN/s)

1b. Network-to-network correlations: Table 1b shows the relationship between EF constructs and ICA network-to-network correlations. Common EF and task set shifting were not significantly associated with network-to-network correlations. Working memory updating was significantly predicted by the correlation between their Left Frontoparietal Control ICN and dmPFC subsystem of default network ($r = -.254, p < .015$). The nature of this relationship is such that greater working memory updating specific executive function is associated with a more negative correlation between the time courses of their Left Frontoparietal Control ICN and dmPFC subsystem of Default ICN. Working memory updating was also significantly predicted by the correlation between their Right Frontoparietal Control ICN and Hubs of Default ICN ($r = .263, p < .012$). The nature of this relationship is such that greater working memory updating specific executive function is associated with a more positive correlation between the time courses of their Right Frontoparietal Control ICN and Hubs of Default ICN.

1c. Dual Regression: Table 1c shows resulting 1- p-value images from the dual regression analysis of the each noted ICA component and EF construct. For each relationship, increased activation of highlighted region (thresholded at $1 - p$ of .995) within or along with the noted network predicted higher EF construct scores.

Figure 2. ICN-to-ICN Correlation Distributions Across Group

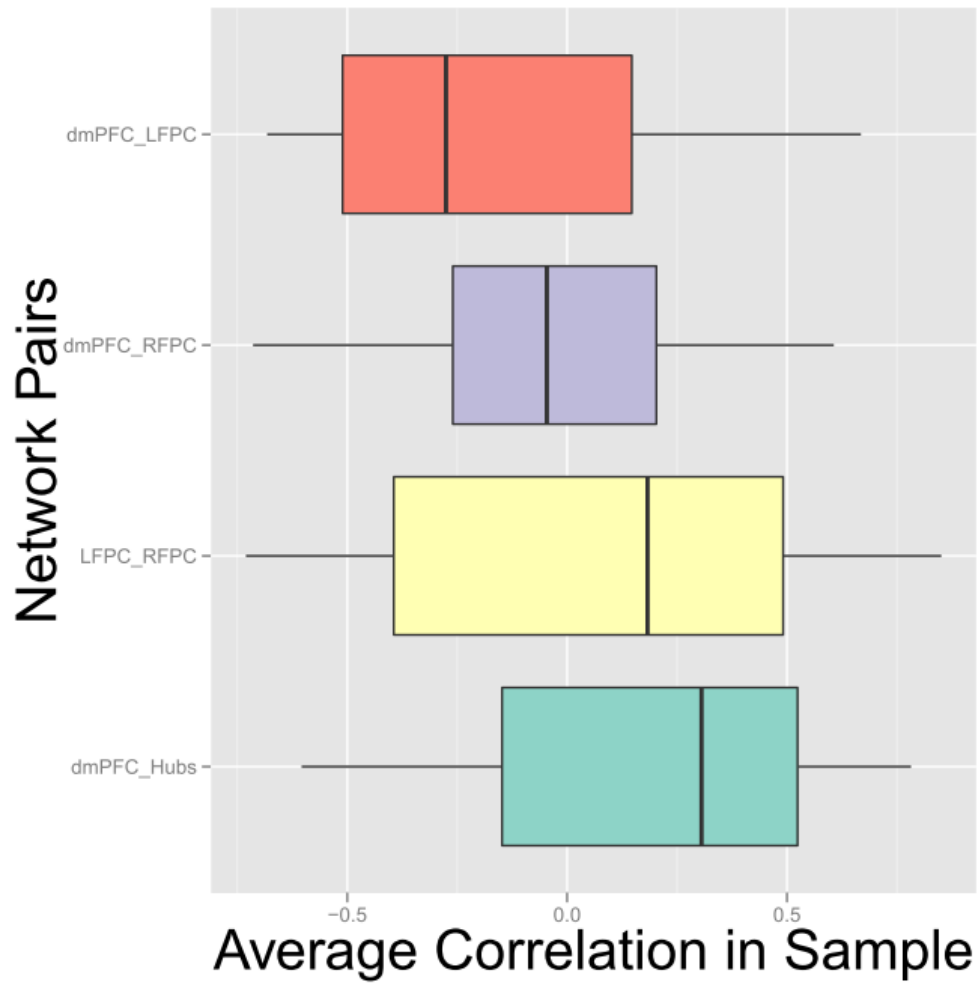


Figure 2 shows the average correlation between sample pairs of ICNs in the current sample.

Discussion

The current study identified relationships between executive function constructs and rs-fMRI through three distinct analyses. We found that not only can activity within a particular ICN predict executive function ability, but the relationship between two ICNs (as assessed by Pearson's coefficient of correlation) and activity within subcomponents of ICNs are also predictors of individual differences in executive function ability.

We predicted that the executive function contrast representing the common component of executive function would be predicted by expression of networks or regions containing anterior prefrontal cortical regions. This hypothesis was motivated by research suggesting that the common component of executive function is mechanistically dependent on the maintenance of goals and abstract tasks set goals, functions that have been localized to the frontal poles (Christoff et al., 2009; Dosenbach et al., 2008). In the primary analysis of subject ICN effect sizes and executive function constructs, we found that activity in the default network is linked to the common component of executive function, such that individuals with larger default network effect sizes at rest were generally better at executive function tasks. It should be noted that the relationship between dmPFC subsystem and common EF was significantly greater than the relationship between visual network and common EF but was not significantly greater than the relationship between the hubs subsystem of the default network and common EF. We refer to this initial finding as between default network and common EF due to this lack of specificity.

At first blush, this finding does not support the hypothesis regarding executive function regions playing a role in maintenance of goals and task sets, as the default network has been associated with "task-negative" activity. However, the follow-up Dual Regression analysis sheds much light allowing for clarity regarding this result. In the Dual Regression analysis, an area in anterior prefrontal cortex (aPFC) emerged as a region that covaried with the dmPFC subsystem of the default network more for

individuals with higher common executive function. So, rather than a network containing the anterior prefrontal cortex predicting executive function, its positive coupling with the default network at rest was predictive of general EF ability such that individuals with the highest general EF ability were those who activated aPFC synchronously with the dmPFC subsystem of the default network. This result suggests cooperation between anterior prefrontal cortex, a region implicated in the maintenance of abstract representation and/or goals, and a subset of default network regions as one factor contributing to greater ability to perform on executive function tasks in general. Previous findings have suggested that individuals utilize these default regions together during the performance of tasks such as autobiographical planning, an activity that requires both executive control and access to brain systems responsible for autobiographical memory (Spreng et al., 2010). Additionally, a combination of default and frontopolar regions has been implicated in processing of both past memories and future plans (Addis, Wong, & Schacter, 2007; Schacter, Addis, & Buckner, 2008). Perhaps individuals with a history of more effective or more frequent prospective planning (associated with coactivation of default and frontopolar regions) are also generally better at tasks that require executive function.

Another prediction was that the diversity aspects of executive function, working memory updating and task set shifting specific executive functions would be predicted by resting state activity in the frontoparietal control networks. This hypothesis was supported: shifting specific and working memory updating specific executive functions were predicted by expression of the right and left lateralized frontoparietal control networks, respectively. However, the lateralization of these effects was not predicted and only working memory updating had a left-side-specific relationship (relationship between RFPC ICN and shifting was not significantly different from LFPC ICN and shifting). And, the opposite lateralization would be predicted based on a study that found working memory updating task-induced activations in bilateral DLPFC but more so in right DLPFC (D'Ardenne et al., 2012). Additionally, TMS to right DLPFC (but not left) slows RT in the same updating task. Further exploration is needed to

reconcile this conflict regarding the lateralization of working memory updating and task set shifting processing.

Another way in which the current results diverge with the existing literature is that all previous studies exploring the relationship between rs-fMRI and individual differences in behavior have found a bilateral frontoparietal control (task-positive) network. When comparing studies the current study to those that have found a relationship with a bilateral frontoparietal control network, there is a large difference in sample size. Perhaps the large n of the current study allowed a more powerful parsing of the resting state data, yielding both LFPC and RFPC ICNs as separate components. Thus, we observed relationships that were not possible to explore with smaller data sets in previous studies.

Of note, the lateralized effects observed in the present study do not appear to be driven by the nature of the material on which these operations are performed. Both the task set shifting and working memory updating paradigms used in the current study relied equally on language, a typically left lateralized process. The reliance on language might have suggested a relationship between activity in left frontoparietal control regions and both shifting and working memory updating executive functions. Similarly, the task set shifting and working memory paradigms each relied heavily on context monitoring, a process that has been described as right lateralized in the past (Chatham et al., 2012). While the current study did find a relationship between RFPC ICN and task set shifting, no relationship between working memory updating and RFPC ICN was observed, which may undermine a context monitoring explanation of the lateralized effects. Hence, the reason for lateralized effects is not clear.

The secondary analysis showed that the network-to-network time course correlations predicted to a significant degree only the working memory updating specific aspect of executive function. Greater working memory updating was associated with a more negative correlation between the time courses of their Left Frontoparietal Control ICN and dmPFC subsystem of Default ICN. The negative relationship

between LFPC and dmPFC subsystem of the default network is an expected finding as similar results have been shown in the past with more general executive function tasks (flanker task; Kelly et al., 2008). We interpret this finding similar to Kelly and colleagues in that negative correlations between default and executive regions might represent a control framework that is highly regulated. Supporting this interpretation is research linking failure to establish an anticorrelated relationship between control and default networks during performance of a task results to lapses of attention (Weissman et al., 2006). Contrary to the negative correlation between LFPC and dmPFC subsystem of the default network predicting better updating, a positive correlation between RFPC and the hubs of the default network was also associated with better updating. One study (Spreng et al., 2010) has shown the coupling of default and frontoparietal control network in the context of an autobiographical planning task that required both access to autobiographical memory and also executive control. However, this result is, to our knowledge, the only example of positive coupling between these two networks. Interpreting this finding is a potential area of exploration for future research as most research has previously highlighted the behavioral relevance of anti-correlations between aspects of the default network and control networks.

We have shown that, within an intrinsic connectivity network, the degree to which an individual activates a given intrinsic connectivity network is associated with the level of an individual's executive function. Does the composition of ICNs also contribute to variation in executive function? Dual Regression analysis yielded one or more regions that covaried across subjects with each measure of executive function. Dual Regression analysis of the LFPC network and working memory updating specific executive function revealed that individual with greater co-activation of middle frontal gyrus and posteromedial prefrontal cortex (bordering anterior cingulate cortex) within the LFPC had better working memory updating specific executive function. These results suggest that coactivation of these areas at rest is especially predictive of updating specific performance. Within the LFPC ICN, these areas

stand out as being frequently implicated in executive function tasks, particularly as sources of bias over task relevant processes/information (MFG) or as assisting in guidance of responses (pmPFC/ACC, Banich, 2009). One important aspect of working memory updating is context processing, so it stands to reason that greater coactivity between regions responsible for the appropriate biasing and guidance of responses, and other executive function regions may be better updaters.

Dual Regression analysis of the RFPC network and task set shifting specific executive function revealed that individual with greater coactivation of an area in left parietal cortex and the RFPC had better task set shifting specific executive function. This finding supports theories of the role of parietal cortex in executive function (e.g. - see Esterman et al., 2009), which proposes parietal cortex as being an important source of control over multimodal sensory information that contributes to the representation of task sets in many different domains of executive function. Parietal cortex has been implicated in many kind of shifting paradigms, such as paradigms involving switching between external stimuli (e.g. – in a spatial attention task) and also between internal thoughts (e.g. - categorization rules; Chiu & Yantis, 2009).

Caveats and Future Directions

One caveat of the current study is the interpretation of resting state functional brain activity as reflecting intrinsic processes in the brain rather than reflecting ongoing internal mentation or other processes. Historically, the interpretation of rs-fMRI as reflecting intrinsic processes been the dominant viewpoint based on studies comparing rs-fMRI within subjects during wakeful rest and also during sleep (Larson-Prior et al., 2009). Given the lack of statistically different relationships between ICNs during wake and sleep, most researchers have accepted that rs-fMRI is likely reflective of the intrinsic functional architecture of the brain. However, there are still a variety of studies suggesting a link between ongoing processing and rs-fMRI (Waites et al., 2005; Tambini, Ketz, & Davachi, 2010; Gordon et al., 2012).

Given the disagreement in interpretation of rs-fMRI, it would be reasonable to suggest an alternative to the interpretation of rs-fMRI as intrinsic processing endorsed in the current study. Individual differences in executive function constructs relate to rs-fMRI due to difference in the internal processes that participants engage in during the task of “rest”. That is, people who, for example, update working memory more fluidly in everyday life may also do so when resting in the scanner when asked to just lie still. Or, individuals who are more skilled in task switching may switch thoughts more while being scanned. There is a great deal of speculation about the nature of spontaneous thought processes at rest; however, there is likely little resistance to the suggestion that all three of the discussed executive function constructs play a role in the direction of thoughts at rest. In fact, one recent study suggested that executive functions are utilized during spontaneous thoughts, which are a type of undirected thinking that likely occurs during resting state scans (Levinson, Smallwood, & Davidson, 2012). This study reported more spontaneous thinking for individuals with high working memory capacity as opposed to those with low working memory capacity during a task that required minimal attentional control. Thus, it seems plausible that high executive function ability could be associated with psychological processes during resting-state scans that are different from those experienced by individuals with low executive function ability.

One potential future direction would help to clarify the contribution of unconstrained mental processes to the relationships observed in the current study. Measures of the degree to which participants experience episodes of mind wandering, spontaneous thoughts, rumination (and other indices of internal mentation) in general and during the actual resting state scan, would allow the statistical control of different frequencies and patterns of internal thought.

Conclusion

The current study is a significant contribution to the literature investigating the behavioral relevance of measures of resting state fMRI. We have shown that individual differences in the abilities that contribute to goal-directed behavior are reflected in the nature of individuals' resting-state brain activity. The current study is ambiguous with regard to causality. One of two interpretations is possible: 1. that different levels of executive function ability can, over time, shape the functional dynamics of the brain, or 2. that variation in the intrinsic dynamics of the resting brain lead to varying levels of executive function. The former interpretation has been emphasized in the past. The mechanisms of executive control are likely highly practiced and used in a variety of different task. Individual who are more practiced with different mechanism of cognitive control likely also have a different history of coactivation between regions responsible of these executive abilities. Our results support a division within activity of the resting brain that is specific to a variety of constructs measuring aspects of executive function.

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