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Cortical Thickness in Fronto-parietal and Cingulo-opercular Networks Predicts Executive Function Performance in Older Adults

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Executive function is broadly defined as a collection of cognitive control processes involving planning, organization, and problem-solving. Executive control systems work in a "top-down" fashion to coordinate previous knowledge, current goals, and expectations, to initiate and maintain an attentional state, to act on information obtained from the senses, and to adjust performance based on feedback (Corbetta & Shulman, 2002; Koechlin, Ody, & Kouneiher, 2003). Under constantly-changing environmental demands, this cognitive domain facilitates purposeful and self-directed behavior and is consistently related to real-world outcomes, including performance of instrumental activities of daily living, functional status, and mortality (Bell-McGinty, Podell, Franzen, Baird, & Williams, 2002; Cahn-Weiner, Boyle, & Malloy, 2002; Johnson, Lui, & Yaffe, 2007; Lerner, Lamb, & Freund, 2010; Lezak, Howieson, Bigler, & Tranel, 2012; Power & Petersen, 2013; Vaughan & Giovanello, 2010). Although executive function is clearly important and widely investigated in both neuroscience and neuropsychology, there is little consistency in the construct operationalization between, and even within, the two fields. Adding to the confusion, studies are often limited to exploration of a particular facet (such as one brain region or one executive measure), thus failing to recognize the multiple processes that underlie this construct. Significant work is still needed to better integrate the understanding of executive function between neuroscience and neuropsychology.

One barrier to examining executive function is that no universally-accepted model of the construct exists. Theorists agree that executive function is a "higher-order" cognitive system that allows for flexible and adaptive behavior in non-routine situations; however, factor analysis and lesion studies indicate that division of this construct into more fundamental sub-processes is also appropriate (Baddeley, 1996; Gilbert & Burgess, 2008; Miller &

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Cohen, 2001; Miyake et al., 2000). Such sub-processes include, but are not limited to initiation, working memory, updating, switching, reasoning, selective attention, and inhibition (Baddeley & Hitch, 1994; Hull, Martin, Beier, Lane, & Hamilton, 2008; Jurado & Rosselli, 2007; Lezak et al., 2012).

Studies of executive function have often been limited by inclusion of only one or two neuropsychological tests, which is problematic given the finding that different tests have been shown to measure different executive subcomponents (Burgess, Alderman, Evans, Emslie, & Wilson, 1998). Some tests that are thought to measure the unitary executive function construct have been found to measure separable sub-processes, and furthermore, some single measures appear to tap multiple executive sub-processes (Chan, Shum, Toulopoulou, & Chen, 2008). Based on a single executive function test, predicting an individual's performance on other such tests—not to mention on complex real-world tasks—remains an elusive feat.

In terms of understanding the neural architecture of executive function, a large body of work supports a relationship between neuropsychological measures and neural substrates within the prefrontal and parietal cortex (Barbey et al., 2012; Collette, Hogge, Salmon, & Van der Linden, 2006; Miller & Cohen, 2001; Miller, 2000). However, there is far from a one-to-one correspondence between particular brain regions and executive functions (Alvarez & Emory, 2006). A major challenge relates to lack of consistency among studies in regards to neural measurements. For example, investigation of the “prefrontal cortex” in one study may include Brodmann's areas not included within another study's operationalization of “prefrontal cortex” (Yuan & Raz, 2014). A recent meta-analysis demonstrated that different brain regions were associated with a single executive measure, secondary to methodological differences in imaging analyses across studies (Jurado & Rosselli, 2007). Interpretability of findings is further undercut by the circumstance that neuroscience and neuropsychology as fields tend to utilize different neuropsychological measurements. Whereas neuropsychologists tend to rely on a fairly standard set of norm-referenced tests, neuroimaging studies commonly use original executive tasks created by the researchers or modify traditional neuropsychological assessments for use in a scanner (Paxton, Barch, Racine, & Braver, 2008; Spreng, Stevens, Chamberlain, Gilmore, & Schacter, 2010; Sridharan, Levitin, & Menon, 2008). Different approaches to measurement of executive function, both in terms of imaging techniques and neuropsychological assessment, clearly present a barrier to cross-field interpretability of findings.

Thus, given any two studies of *executive function*, we may be left with several questions: Were the same executive sub-processes actually measured in each study? Might differences between studies relate to differences in researchers’ approach to defining brain structures? What can neuroimaging results tell neuropsychologists about how their clients might perform on traditional neuropsychological assessments? Better understanding of executive function will come about through refinement of neuroimaging and neuropsychological methods for clarity and consistency.

The present study used the well-established dual-network model of executive function (Dosenbach et al., 2006, 2007; Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008) as a frame to guide the investigation of the relationship between neural substrates and executive function performance in a sample of healthy older adults. As opposed to a unitary framework, the dual-network model of executive function posits two separate but strongly intra-connected brain networks: the *fronto-parietal (F-P) network* and the *cingulo-opercular (C-O) network*. As shown in Table 1, nodes in the F-P network include bilateral frontal cortex, bilateral intraparietal sulcus (IPS), bilateral precuneus, middle cingulate cortex (mCC), bilateral inferior parietal lobule (IPL), and bilateral dorsolateral prefrontal cortex (DLPFC). Situated spatially between the default mode network (inwardly-directed attention) and the dorsal attention network (externally-oriented attention), the F-P network may functionally connect both for the purposes of information integration, a key feature of executive function (Elton & Gao, 2014; Vincent, Kahn, Snyder, Raichle, & Buckner, 2008). The second executive component, the C-O network, includes the anterior insula/frontal operculum (aI/fO), dorsal anterior cingulate cortex/medial superior frontal cortex (dACC/msFC), and anterior prefrontal cortex (aPFC). This collection of regions is thought to be a core task set system for the sustained, domain-independent control of externally-directed tasks.

Understanding the relationship between the anatomy of these executive function regions and performance on executive function tasks was central to the present study. There are several techniques available to investigate cortical anatomy, including measurement of the surface area of an area of cortex, the cortical thickness at a given location, and the volume of an area of cortex (surface area x thickness). The present study was focused on regions in frontal and parietal brain areas because of their involvement in executive control. Given the considerable controversy about how to define the extent of each of these cortical areas (Cohen et al., 2008; Yeo et al., 2011), we chose to measure cortical thickness in the pre-defined regions of interest. Measurement of gray matter volume, as a function of both surface area and cortical thickness, would confound understanding of the independent influence of each of these cortical anatomy features (Panizzon et al., 2009; Winkler et al., 2010). In addition, it has been shown that cortical thickness may be a more sensitive indicator of age-associated gray matter change compared to volumetric measurement (Hutton, Draganski, Ashburner, & Weiskopf, 2009; Winkler et al., 2010), an issue that is important given the current sample. Hence, cortical thickness was the best option to explore relationships between anatomy and executive function performance in the brain regions of interest in the present study.

Unique to this investigation, exploratory factor analysis was used to elucidate the nature of executive processes tapped by the present neuropsychological battery. This method was chosen to address the problem of ambiguous measurements noted in the literature (Yuan & Raz, 2014). In sum, this study bridged neuroscience and neuropsychology perspectives in the pursuit of a more cohesive understanding of *executive function*, guided by (1) the dual-network neural model of executive control processes (2) examination of cortical thickness, a sensitive indicator of age-related gray matter change, and (3) a data-driven approach to characterize executive function performance.

Method

Participants

Forty-one right-handed, community-dwelling older adults residing in the Birmingham, Alabama, metropolitan area were recruited through mailings, flyers, and from medical clinics at the University of Alabama at Birmingham (UAB) for participation in the Visual Integrity and Neural plasticity in the Elderly Study (VINES). The UAB Institutional Review Board approved all experimental procedures, and written informed consent was obtained. Exclusion criteria included: corrected far visual acuity of worse than 20/40, inability to complete a modified Useful Field of View (UFOV) task with at least 60% accuracy, evidence for dementia (via self-reported diagnosis and/or TICS-M < 21), self-reported previous serious head injury, loss of consciousness for >2 minutes, history of neurological disorder, history of hallucinations or delusions, current use of psychoactive medications, and current or remote history of substance abuse. For scanning purposes, potential participants were excluded if they weighed more than 300 pounds, had a girth measuring more than 60 inches, suffered from claustrophobia, or had ferromagnetic implants or other contraindications to the MRI environment. Sample descriptives are provided in Table 2.

Measures

Useful Field of View (UFOV®) test—UFOV® (Ball & Roenker, 2014) is a computerized cognitive test that assesses processing speed, ability to divide attention, and ability to ignore irrelevant stimuli (Edwards et al., 2006). UFOV scores for each subtest reflect the stimulus display speed (17-500 ms) at which the individual can correctly complete the task 75% of the time. Three subtests were included in the current analyses. UFOV1 assesses processing speed through presentation of a central stimulus which participants are asked to identify (e.g., car or truck). UFOV2 assesses divided attention through simultaneous presentation of a central identification stimulus (e.g., car or truck) and peripheral localization stimulus (e.g., 'Where was the outside car?'). UFOV3, a selective attention task, is identical to the UFOV2 task, except that it requires participants to ignore distractor stimuli which appear in concentric rings around the central stimulus and in all peripheral locations except that occupied by the peripheral stimulus. UFOV has high test-retest reliability and validity, and normative data for comparison across age and education groups is available (Edwards et al., 2005, 2006). Lower scores on the UFOV subtests represent better performance (faster accurate performance).

Complex Reaction Time/ Road Signs Test (CRT)—CRT is a computerized task which measures processing speed and inhibition of complex visual information. Used in the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study, a large, multi-site randomized clinical trial of three cognitive interventions, the CRT involves presentation of various road signs (Ball, Beard, Roenker, Miller, & Griggs, 1988; Edwards et al., 2005; Owsley, Sloane, McGwin, & Ball, 2002; Roenker, Cissell, Ball, Wadley, & Edwards, 2003). Participants are instructed to respond as quickly as possible, and in characteristic ways, to road signs without slashes: click the mouse if the sign shows a pedestrian or bike; move the mouse to the left if the sign shows a left-pointing arrow; move the mouse to the right if the sign shows a right-pointing arrow. Participants are to inhibit their responses to signs with slashes through them. Twelve trials of three road signs and twelve trials of six road signs are presented. The average reaction time across all trials (three-stimulus and six-stimulus presentations) was calculated (Jobe et al., 2001).

Controlled Oral Word Association Test (COWAT): FAS—The COWAT (Benton, Hamsher, & Sivan, 1994) is a measure of phonemic fluency, or the ability to generate fluent speech (Lezak et al., 2012). An examiner presents participants with a letter of the alphabet (e.g. “F”), and instructs them to verbalize as many words as they can starting with that letter, within the time frame of one minute. Participants are instructed to avoid giving proper nouns and the same word with different endings. This procedure is repeated with two additional letters.

Animal Fluency—Animal fluency is a measure of semantic fluency, or the ability to generate words within a given category (Lezak et al., 2012). Participants are asked to name as many animals as they can in one minute.

Matrix Reasoning—The Matrix Reasoning subtest of the Wechsler Abbreviated Scale of Intelligence (WASI) is a measure of non-verbal fluid reasoning (*Wechsler Abbreviated Scale of Intelligence Manual*, 1999). Participants are presented with a figure in which one piece is missing. They are asked to select the missing piece from several possible alternatives, that is, to choose the piece that will best complete the pattern or visual analogy.

Imaging Procedures

Magnetic Resonance Imaging (MRI) acquisition—MR imaging was collected at the Civitan International Research Center Functional Neuroimaging Research Lab. A high-resolution T1-weighted MPRAGE image (TE = 2.6ms, voxel size 1 ×1 × 1.1 mm) was acquired for each participant in a 3T head-only Siemens Allegra scanner.

Analysis of cortical thickness in FreeSurfer—Analysis of cortical thickness at predefined regions of interest (ROI) was conducted with FreeSurfer Image Analysis Suite Version 5.3.0 (on a Linux Mint operating system), a freely-available set of tools (http://surfer.nmr.mgh.harvard.edu/) for automated surface-based reconstruction and visualization of cortical structure. In-depth discussion of the FreeSurfer suite is available in other publications (Dale, Fischl, & Sereno, 1999; Fischl & Dale, 2000; Fischl, Sereno, & Dale, 1999).

Because we had established *a priori* ROI based on the executive control network proposed by Dosenbach and colleagues (2007), the central Talairach coordinate for each region was used to find the nearest vertex in FreeSurfer's tksurfer tool with the *select_talairach_point* command. This vertex served as the center of a region of interest that was created in FreeSurfer space. This single vertex was expanded using the FreeSurfer “Dilate Label” function, which expands the region to include the original vertex and all neighboring vertices. This process of dilation was repeated for each region a total of three times, and an identical dilation procedure was repeated with each of the predefined ROI. A total of 3 dilations for each region was chosen because the resulting surface-based ROI had a mean surface area of 30 mm^2, which corresponds to a circle with a diameter of roughly 6 mm.

This size was chosen because it is large enough to be meaningful given our voxel acquisition size of 1 mm^3, but small enough that the region was unlikely to encompass other functional areas. Table 1 lists the mean surface area for each ROI.

Statistical Analyses

Imaging analyses—Composite cortical thickness scores were created for the *a priori* defined F-P and C-O networks. First, each participant's mean whole-brain cortical thickness was used to normalize his or her cortical thickness measurement in individual ROI. Then, normalized ROI values contributing to the F-P and C-O networks respectively were averaged to create the two network composite scores.

Cognitive analyses—This investigation was a secondary data analysis of neuropsychological assessments administered as part of the VINES study. All executive function measures included in the VINES test battery were considered in the present analyses. Visual inspection of the data revealed no apparent violations of the assumptions of homoscedasticity, linearity, and normality, except for UFOV1 scores, which were highly positively skewed (Skewness = 3.25). Due to its high positive skewness, UFOV1 was dropped from further analyses. No cases of missing or erroneous data were identified for any test variable ($N = 41$).

An exploratory factor analysis of the executive function measures was performed with varimax rotation in SPSS (Version 22). Variables analyzed included UFOV2, UFOV3, CRT average, COWAT total, Animal Naming total, and WASI Matrix Reasoning T-score. Bartlett's test of sphericity was significant ($\chi^2 = 48.730$, $p < .001$), indicating sufficient correlation between the variables to proceed with the analysis. Number of factors was not specified. Only eigenvalues greater than one were extracted.

Based on inspection of the scree plot and extracted rotated factors, the analysis yielded two factors: complex attention control (CAC) and sustained executive control (SEC). Factor composite scores for CAC and SEC were calculated from weighted averages for the regression analyses.

Combined analyses—Two multiple linear regressions were conducted, with the F-P and C-O composite cortical thickness measurements entered as independent variables. The CAC composite score served as the dependent variable in one regression model, and the SEC composite score served as the dependent variable in a second model. Consideration of covariates was guided by literature which indicated that demographics (gender, age, race, and education), emotional status (self-reported depression), cortical thickness, and cognition are related (Austin, Mitchell, & Goodwin, 2001; Daniel et al., 2013; Duda, Puente, & Miller, 2014; Gallo, Rebok, Tennstedt, Wadley, & Horgas, 2003; Kim et al., 2012; Rexroth et al., 2013). Self-reported depression (CES-D total score) was excluded based on its highly positive skew (Skewness = 1.146) and the observation that no participant reported a clinically significant level of depression (defined as a score > 16; See Table 2). Greater cortical thickness in F-P and C-O networks was significantly correlated with Caucasian race and higher education (See Table 4). No other significant correlations were observed. Race and education were entered as covariates in both linear regression models. A region in the motor cortex associated with the right foot was selected as a control region, due to its expected lack of involvement in executive functioning. The motor control region was not significantly predictive of CAC (p =.257) or SEC (p =.468), supporting the validity of the findings; this region was excluded from the final models.

Results

As seen in Table 2, participants in the present study were generally healthy, well-educated older adults with low reported levels of depressive symptomology. The sample was well-balanced in terms of gender representation and was predominantly Caucasian. A reasonable amount of variability among participants' performance was observed for all executive function measures (Table 2).

Results of the Factor Analysis of Executive Function Measures

Given the heterogeneous nature of the executive function construct, exploratory factor analysis was employed to investigate whether individual cognitive measures of executive function loaded onto separable factors. As seen in Table 3, measures cleanly loaded onto two factors. UFOV2, UFOV3, and CRT average strongly loaded onto Factor 1. These measures require response to a sequence of complex, quickly-presented stimuli, and subtle indicators of performance are given (e.g., faster stimulus presentation speed with correct UFOV response or a pausing of CRT until a response is made). To reflect this set of task demands, Factor 1 was named Complex Attention Control (CAC). COWAT, Animal Naming, and Matrix Reasoning tasks strongly loaded onto Factor 2. These measures require the maintenance and manipulation of information within an organizational framework in order to generate solutions. That is, participants must hold in mind a rule about a letter, category, or visual puzzle while generating material which correctly fits within those parameters. No indicators about one's performance are provided. Factor 2 was named Sustained Executive Control (SEC) to reflect this set of task demands.

Results of Combined Analyses

Greater cortical thickness in the F-P network, but not the C-O network, significantly predicted better (faster) performance on the CAC cognitive factor (See Table 5). Conversely, greater cortical thickness in the C-O network, but not the F-P network, significantly predicted better performance (higher scores) on the measures comprising the SEC cognitive factor. Figure 2 displays this double dissociation with a plot of cortical thickness values in each network across each cognitive factor. In the final models, participant race and education were also significant predictors of cognitive performance, such that having more education and Caucasian race predicted better performance on both cognitive composites. In addition, when the control region of interest (motor cortex) was entered in the models, it did not significantly contribute to the prediction of executive function, lending support to the validity of the present findings. In sum, these results indicate that cortical thickness in distinct components of the executive control network differentially predicts performance on tasks with separable executive demands.

Discussion

Though the term *executive function* is frequently discussed in neuroscience and neuropsychology, the complex construct has been hypothesized to encompass a host of subcomponents including initiation, working memory, updating, switching, reasoning, selective attention, and inhibition. The principal aim of this study was to examine the relationships between cortical thickness in the F-P and C-O networks of the dual-component model of executive function and actual performance on a battery of executive neuropsychological measures. Results indicated a remarkably clean double dissociation between cortical thickness in the two networks and performance on two data-derived executive factors, called CAC and SEC. Average cortical thickness across regions comprising the F-P network predicted performance on the CAC factor, but not the SEC factor. Conversely, average cortical thickness across regions comprising the C-O network predicted performance on the SEC factor, but not the CAC factor. All relationships were in the expected direction, such that greater cortical thickness predicted better performance. Furthermore, the pattern of double dissociation aligned with the proposed function of the F-P and C-O networks based on functional imaging studies suggesting that the FP network is involved with adaptive, online control whereas the C-O network is involved in stable control of task set over sustained tasks.

The Complex Attentional Control (CAC) Factor

Participants' UFO2, UFOV3, and CRT average scores cleanly loaded onto one factor. These tasks share fundamental demands. First, all involve directing attention to perceptual information. All tasks in this factor present stimuli for brief periods (e.g., 17-500 ms for UFOV2 and UFOV3) or rapidly shift in content and location across successive trials (CRT). Second, subtle information about task performance is provided by the tasks (e.g., the UFOV tasks slow down when errors are made, and the CRT test does not continue until correct response is made). The factor encompassing UFOV2, UFOV3, and CRT performance was called *Complex Attention Control (CAC)* to reflect the tasks' shared fundamental requirements of attentional initiation, allocation, and behavioral adjustment in response to task performance feedback. The time course of task demands evolves on a moment-to-moment basis.

Greater cortical thickness in the F-P network, but not the C-O network, predicted better performance on the CAC factor. The relationship between F-P cortical thickness and this data-driven executive factor supports Dosenbach and colleagues' functional imaging-derived conceptualization of the F-P as an adaptive control network. They found that lateral frontal and parietal brain regions of the F-P network showed transient start-cue and error-related signals (Dosenbach et al., 2006), and that these regions correlated strongly with one another in a resting state functional connectivity analysis (Dosenbach et al., 2007). The current study demonstrated that the cortical thickness of these regions also predicts performance on neuropsychological tasks with complex attention demands.

The Sustained Executive Control (SEC) Factor

Participants' COWAT, Animal Naming, and Matrix Reasoning scores cleanly loaded onto a second factor. These tasks require sustained attention to maintain task set and problem-solve. For example, on the COWAT, participants are instructed to "generate as many words that start with the letter 'F' as you can think of in one minute" while adhering to two additional rules: (1) generated words must not be proper nouns, and (2) the same word with different endings (e.g. friend, friends, friendly) cannot be used. Thus, COWAT and Animal Naming require the application of multiple task rules simultaneously, that information not explicitly provided be accessed, and that answers be within the bounds of the task parameters. Similarly, in the Matrix Reasoning task participants are required to evaluate potential answers based on "rules" or "patterns" in the given figure which are not explicitly provided. All three tasks demand manipulation of information over a rather long time course (i.e. minutes vs. seconds) and in the absence of performance feedback. To reflect the fundamental task component concerned with self-initiated and maintained goal maintenance across task performance, this factor was called *Sustained Executive Control (SEC)*.

Greater cortical thickness in the C-O network, but not the F-P network, predicted better performance on the SEC factor. This is in line with Dosenbach's proposed role of the C-O network, as one of stable set maintenance across implementation of task set. Dosenbach and colleagues (2006, 2007) found sustained medial frontal/cingulate cortex and bilateral anterior insula signals across task conditions which were correlated strongly in a resting state functional connectivity analysis. Other researchers have confirmed that regions in the C-O network (dACC, bilateral insula, and frontal cortex) show increased tonic activity for the duration of tasks, supporting the idea that the C-O network serves to guide ongoing function (Simões-Franklin, Hester, Shpaner, Foxe, & Garavan, 2010). Further, the anterior insula/frontal operculum, an element of the C-O network, is not recruited by tasks driven by perceptual information, such as the CAC tasks (Dubis, Siegel, Neta, Visscher, & Petersen, 2014). Some have deemed the C-O network "the salience network," as it filters and discards irrelevant stimuli streaming in from internal and external sources in favor of information relevant to ongoing behavior (Menon & Uddin, 2010; Seeley et al., 2007). For example, in a study by Vaden et al. (2013) C-O network engagement was associated with optimal performance in difficult listening conditions (recognizing poorly intelligible speech). Increased C-O activity was associated with increased likelihood of correct word recognition, taken to mean that the C-O network continuously monitors performance throughout a task by serving to enhance task-related attention and suppress irrelevant internal or external stimuli. This interpretation would certainly agree with the findings of the present study, because tasks loading on the SEC factor demanded task maintenance over time under conditions of uncertainty about task performance (i.e. no indicators or performance).

Significance of Current Findings

In sum, results suggest that the unified concept of *executive function* is an amalgam of separable fundamental sub-processes, and that performance may be predicted by cortical thickness of distinct brain networks. This is a unique and valuable finding for multiple reasons. First, a notable limitation of several neuroimaging studies to date has been reliance on correlating brain regions with a single cognitive measure, which likely under-represents the complexity of the executive function construct, as well as its relationship with identified brain regions. The most accurate picture of an individual's executive functioning will emerge only after considering and integrating data from multiple measures. *Executive function* in the present study was defined in a data-driven manner, based on a battery of measures which cleanly loaded onto two factors. It is possible that a different battery of measures would have yielded slightly different factors; however, including multiple measures is a step forward in terms of attempting to capture a thorough index of participants' executive functioning abilities.

Second, the two cognitive factors identified in the present study showed a remarkably clean double dissociation in their relationships to established neural networks, based on existing functional imaging findings (Dosenbach et al., 2006, 2007, 2008). In addition, the task demands of each cognitive factor aligned with the functional roles of their associated networks, as postulated by Dosenbach and colleagues, among others. That is, cortical thickness of the F-P network, hypothesized in functional imaging studies to be involved in moment-to moment processing, was found to predict performance on measures with task demands involving speedy processing and indicators of task performance. Cortical thickness of the C-O network, hypothesized in functional imaging studies to be involved in maintaining performance throughout the duration of a task, was found to predict performance on tasks evolving over longer time-courses and where indication of performance was not provided.

Furthermore, much of the work done to identify distinct executive networks has been conducted with functional imaging studies. The results of this investigation demonstrate that executive function performance, as measured by neuropsychological tests, relates to the thickness of gray matter in the functionally-identified brain networks. Relative loss or sparing of gray matter in each component of the executive function network may produce various constellations of deficits. The finding of localizable structure-function relationships is exciting in terms of its implications for clinical estimation of cognitive dysfunction or decline and the potential to track the effects of interventions aimed at improving or slowing executive function decline.

Limitations

Limitations of the current study include small sample size and limited statistical power. While a sample size of $N = 41$ is generally adequate for imaging studies, it is small for an investigation of neuropsychological outcomes, and results should be confirmed in a larger sample. Furthermore, while treating cortical thickness across the nodes in each executive network component as a structural unit lent power to the analysis, it ignores the idea that nodes within each network might contribute in unique and independent ways to executive functioning. Some functional studies have suggested that the F-P network may be fractionated further according to functional specialization (Dodds, Morein-Zamir, & Robbins, 2011; Hampshire, Thompson, Duncan, & Owen, 2011), for instance, that the frontal cortex and IPS may be more involved with initiation of task set and top-down distribution of visual attention (Corbetta & Shulman, 2002; Dosenbach et al., 2007), the precuneus and midcingulate with allotment of selective attention, and the DLPFC with processing of error-related signals (Dosenbach et al., 2007). Correspondingly, research has also suggested that specific nodes within the C-O serve specialty functions: For example, the anterior insula may serve to detect the signal in the noise, while the anterior cingulate may play a larger role in set maintenance (Sridharan et al., 2008).

In a similar vein, although we identified two fundamental task components among the neuropsychological battery in a data-driven fashion, it is possible that the inclusion of different measures would have yielded different results. Future research should extend and refine the current investigation to illuminate more precise relationships between the structure of executive function networks and manifest executive performance.

One might observe that the cognitive factors yielded in the present study were split by response format (computer for CAC vs. human administration for SEC). We hypothesize that, rather than the driving force behind the two factors, response format is an artifact of the fundamental task processes they address. The assessments contributing to the CAC factor (UVOV2, UFOV3, and CRT average) were computer-administered, but more importantly involved speeded performance and an element of feedback (e.g., tasks became easier if done incorrectly). Computer administration is preferred for these types of assessments given stimuli type and precise timing measurement. The assessments contributing to the SEC factor (COWAT, Animal Fluency, and Matrix Reasoning) were administered by a trained human tester, but the more important aspect may be that all tasks demanded sustained executive control over a longer period of time, without the benefit of performance feedback. We argue that factors are differentiated by the non-equivalency of their executive demands, and that the response format is simply a function of how these separate demands are best measured.

Conclusion

The methodological approach of this study is valuable, as it was not limited by the specificity of individual neuropsychological measures, but rather contributed to our understanding of task demands in a data-driven manner. In addition, the diverse battery of neuropsychological measures was related to neural structure, within the framework of a well-established, functionally-derived model of executive control. Although executive function is a broad and complex domain, the results of the present study suggest that it may be broken down into more basic, fundamental processes involving moment-to-moment responses to perceptual information and maintenance of information across the span of a task. Furthermore, these fundamental processes are differentially related to distinct neural networks, such that cortical thickness is predictive of cognitive performance. Continued collaboration between neuroscience and neuropsychology researchers will be important to build upon such exciting findings and extend our understanding of the relationships between brain structures and cognitive functioning.

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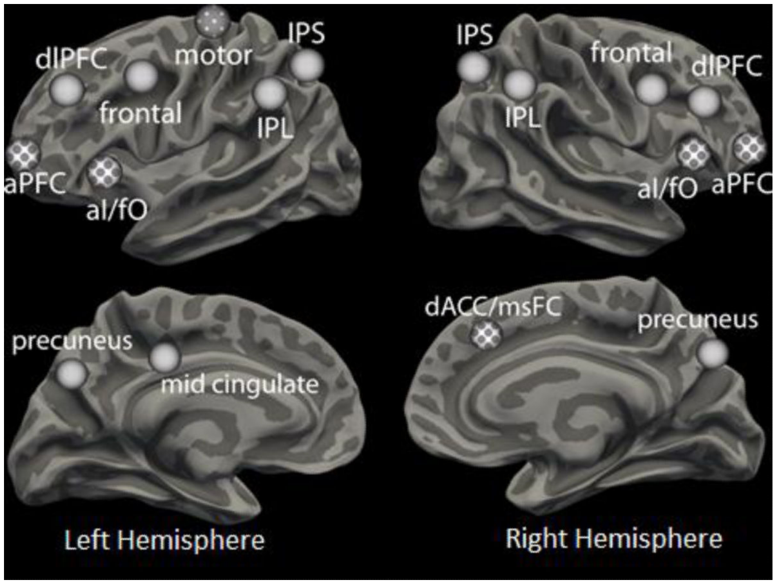

Figure 1.

Spheres represent the location of regions of interest in the fronto-parietal (*F-P*) network (solid), cingulo-opercular (*C-O*) network (large dots), and control region of the motor cortex (small dots). Note that the extent of the sphere is larger than the actual region of interest drawn in FreeSurfer.

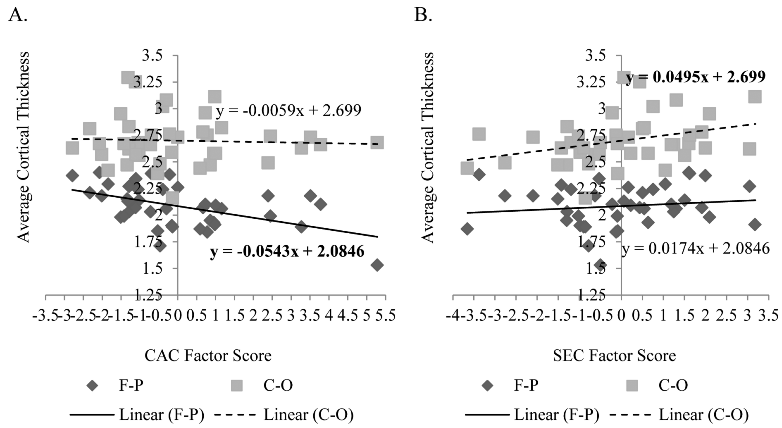

Figure 2.

A) Average cortical thickness in Fronto-parietal (*F-P*) and Cingulo-opercular (*C-O*) networks, plotted against the Complex Attention Control (*CAC*) factor score. The CAC factor score is reflective of time to complete task. Therefore, a higher CAC factor score is indicative of worse performance. Relationship to the F-P network was significant when other factors are accounted for (See Table 5). *B)* Average cortical thickness in F-P and C-O networks, plotted against the Sustained Executive Control (*SEC*) factor score. The SEC factor score is reflective of items answered correctly. Therefore, a higher SEC factor score is indicative of better performance. Relationship to the C-O network was significant when other factors are accounted for (See Table 5).

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Table 1

A Priori Regions of Interest (ROI) Based on Dosenbach et al.'s (2007) Dual-Network Model of Executive Control

ROI	Talairach coordinates			Size (mm^2)
Fronto-parietal (F-P) component	**x**	**y**	**z**	
Right Intraparietal Sulcus	30	−61	39	31
Left Intraparietal Sulcus	−31	−59	42	30
Right Frontal Cortex	41	3	36	31
Left Frontal Cortex	−41	3	36	31
Right Precuneus	10	−69	39	29
Left Precuneus	−9	−72	37	30
Midcingulate	0	−29	30	29
Right Inferior Parietal Lobule	51	−47	42	34
Left Inferior Parietal Lobule	−51	−51	36	32
Right Dorsolateral Prefrontal Cortex	43	22	34	33
Left Dorsolateral Prefrontal Cortex	−43	22	34	32
Cingulo-opercular (C-O) component				
Right Anterior Insula/Frontal Operculum	36	16	4	29
Left Anterior Insula/Frontal Operculum	−35	14	5	28
Dorsal Anterior Cingulate / Medial Superior Frontal Cortex	−1	10	46	24
Right Anterior Prefrontal Cortex	27	50	23	32
Left Anterior Prefrontal Cortex	−28	51	15	31
Control region				
Right Foot Motor Cortex	−8	−38	76	23

Table 2

Participant Descriptives

Variable	*M*	*SD*	Range
Age	71.07	4.64	65-86
Years of Education	15.59	2.80	12-20
CES-D Total Raw	2.95	2.88	0-12
F-P Cortical Thickness (mm)	2.09	0.19	1.53-2.40
C-O Cortical Thickness (mm)	2.70	0.23	2.16-3.29
Control Region Cortical Thickness (mm)	2.18	0.43	1.52-3.09
Whole-brain Cortical Thickness (mm)	2.26	0.10	2.04-2.47
UFOV Subtest 1 (ms)	22.41	15.50	17-87
UFOV Subtest 2 (ms)	118.32	81.954	20-350
UFOV Subtest 3 (ms)	246.05	90.922	83-500
CRT Average (sec)	1.937	0.382	1.329-3.070
COWAT Total Raw	39.37	10.716	20-61
Animal Naming Total Raw	18.88	4.389	9-28
Matrix Reasoning T-Score	60.95	9.343	35-75

		Frequency	Percent
Gender	Men	19	46.3
	Women	22	53.7
Race	Caucasian	33	80.5
	African-American	8	19.5

Note: N = 41 for all variables. *CES-D:* Center for Epidemiological Studies Depression Scale; *F-P*: Fronto-parietal network; *C-O*: Cingulo-opercular network; *UFOV:* Useful Field of View; *CRT:* Complex Reaction Time Test; *COWAT:* Controlled Oral Word Association Test

Table 3

Factor Structure of Executive Function Battery

Factor Items	Rotated Factor Loadings		Communalities
Factor 1: Complex Attention Control (CAC)	1	2	h^2
UFOV2	.802	−.008	.643
UFOV3	.810	.017	.656
CRT Average	.672	−.290	.536
Factor 2: Sustained Executive Control (SEC)			
COWAT	.117	.814	.676
Animal Naming	−.121	.689	.489
Matrix Reasoning	−.454	.622	.593

Table 4

Correlation Among Demographic, Cortical Thickness, and Cognitive Variables

	Gender	Age	Caucasian Race	Education	F-P Cortical Thickness	C-O Cortical Thickness	Control Cortical Thickness	CAC Composite	SEC Composite
Gender	1								
Age	.004	1							
Caucasian Race	−.087	−.059	1						
Education	.161	.064	.037	1					
F-P Cortical Thickness	−.074	−.095	−.058	.295	1				
C-O Cortical Thickness	.109	.141	−.112	−.149	−.299	1			
Control Cortical Thickness	.013	−.009	−.093	−.011	.113	.074	1		
CAC Composite	−.120	.118	−.521**	−.478**	−.476**	.134	.113	1	
SEC Composite	−.063	−.083	.453**	.371*	−.010	.192	.023	−.260	1

Note: F-P: Fronto-parietal network; *C-O*: Cingulo-opercular network; *CAC*: Complex Attention Control; *SEC*: Sustained Executive Control

** Correlation is significant at the 0.01 level (2-tailed)

* Correlation is significant at the 0.05 level (2-tailed)

Table 5

Cortical and Demographic Predictors of Cognitive Factors

	Model 1 Dependent Variable: Neuropsychological Factor CAC				**Model 2 Dependent Variable: Neuropsychological Factor SEC**			
Predictor Variables	***B (SE)***	**95% CI**	β	***p***	***B (SE)***	**95% CI**	β	***p***
Constant	18.88 (4.27)	[10.23, 27.53]		<.001	−11.14 (4.74)	[−20.75, −1.53]		.024
Caucasian Race	−2.43 (0.45)	[−3.34, −1.52]	−0.55	<.001	1.83 (0.50)	[0.82, 2.85]	0.47	.001
Education	−0.22 (0.07)	[−0.36, −0.09]	−0.35	.002	0.22 (0.07)	[0.07, 0.37]	0.40	.005
Cortical Thickness F-P Network	−11.73 (2.91)	[−17.64, −5.82]	−0.44	<.001	−0.26 (3.24)	[−6.82, 6.31]	−0.01	.937
Cortical Thickness C-O Network	−2.23 (2.16)	[−1.70, 1.67]	−0.11	.308	5.37 (2.40)	[0.52, 10.23]	0.30	.031

Full Model	***F***	**Adjusted R^2**	***p***	***F***	**Adjusted R^2**	***p***
	16.22	0.603	<.001	6.54	0.356	<.001

Note: F-P: Fronto-parietal; *C-O:* Cingulo-opercular; *CAC*: Complex Attention Control; *SEC*: Sustained Executive Control