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Multimodal neural correlates of cognitive control in the Human Connectome Project

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ABSTRACT

Cognitive control is a construct that refers to the set of functions that enable decision-making and task performance through the representation of task states, goals, and rules. The neural correlates of cognitive control have been studied in humans using a wide variety of neuroimaging modalities, including structural MRI, resting-state fMRI, and task-based fMRI. The results from each of these modalities independently have implicated the involvement of a number of brain regions in cognitive control, including dorsal prefrontal cortex, and frontal parietal and cingulo-opercular brain networks. However, it is not clear how the results from a single modality relate to results in other modalities. Recent developments in multimodal image analysis methods provide an avenue for answering such questions and could yield more integrated models of the neural correlates of cognitive control. In this study, we used multiset canonical correlation analysis with joint independent component analysis (mCCA + jICA) to identify multimodal patterns of variation related to cognitive control. We used two independent cohorts of participants from the Human Connectome Project, each of which had data from four imaging modalities. We replicated the findings from the first cohort in the second cohort using both independent and predictive analyses. The independent analyses identified a component in each cohort that was highly similar to the other and significantly correlated with cognitive control performance. The replication by prediction analyses identified two independent components that were significantly correlated with cognitive control performance in the first cohort and significantly predictive of performance in the second cohort. These components identified positive relationships across the modalities in neural regions related to both dynamic and stable aspects of task control, including regions in both the frontal-parietal and cingulo-opercular networks, as well as regions hypothesized to be modulated by cognitive control signaling, such as visual cortex. Taken together, these results illustrate the potential utility of multi-modal analyses in identifying the neural correlates of cognitive control across different indicators of brain structure and function.

1. Introduction

Cognitive control refers to the set of cognitive functions that are employed to encode and maintain task representations so as to regulate one's thoughts and actions (Botvinick and Braver, 2015). These functions are accomplished through the recruitment of neural systems that are also involved in supporting memory, perception, attention, action selection and inhibition, among other functions (Miller and Cohen, 2001; Botvinick and Braver, 2015). Together, these functions enable and regulate the decision-making processes that are omnipresent in life. Within the

Abbreviations: mCCA + jICA, Multiset canonical correlation analysis with joint independent component analysis; IC, Independent component.

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neuroimaging literature, several different imaging modalities have been used to study the neural underpinnings of cognitive control, including structural, functional, and resting state MRI. However, in much of the literature, a single neuroimaging modality is examined in a given study. This can make it difficult to understand how findings in different modalities relate to each other and to cognitive control. Thus, the goal of the present study was to use a data-driven multimodal analysis approach to study the neural correlates of cognitive control.

1.1. Single imaging modality studies

As noted above, much of the existing literature on the neural correlates of cognitive control have examined one imaging modality in a particular study. For example, a meta-analysis of 31 studies of cortical volume and 10 studies of cortical thickness in prefrontal cortex (PFC) revealed a moderate positive relationship between overall PFC volume and better cognitive control performance (Yuan and Raz, 2014), with subregion analyses suggesting stronger relationships in lateral and medial PFC versus orbitofrontal cortex. Further, there was a significant relationship between PFC thickness and cognitive control, though there were not enough studies to examine the relationship between the thickness of subregions of PFC and cognitive control. Additional studies not included in this meta-analysis are consistent with these findings (Burzynska et al., 2012; Tu et al., 2012), though the specificity of such relationships to PFC remains an open question.

Additionally, various forms of functional MRI (fMRI) have also been used to study cognitive control. While a full review of the task fMRI (tfMRI) literature is beyond the scope of this introduction (see (Niendam et al., 2012; Botvinick and Braver, 2015; D'Esposito and Postle, 2015), among others), meta-analytic evidence from this literature also strongly implicates prefrontal cortex areas as critical to cognitive control (Niendam et al., 2012). Drawing from 193 studies of cognitive control in healthy participants, Niendam and colleagues identified robust activation in lateral and medial prefrontal, dorsal anterior cingulate, and parietal cortex in response to a broad set of cognitive control paradigms. Further, they divided the studies into specific domains of cognitive control, which identified differential patterns of activation across these same areas as well as portions of the basal ganglia and cerebellum.

Resting state functional connectivity MRI (rsfcMRI) has also been used to study the neural correlates of cognitive control. For example (Cole et al., 2012), used global brain connectivity, a measure of a region's connectivity with the rest of the brain, to identify a region in lateral prefrontal cortex wherein resting activity was highly correlated with fluid intelligence, an index related to cognitive control (Seeley et al., 2007). used an ROI and ICA based approach to rsfcMRI and identified clusters in bilateral intraparietal sulcus that positively correlated with better cognitive control. Further, recently developed methods in dynamic rsfcMRI (Calhoun et al., 2014) have identified specific modes of neural resting-state connectivity and that inter-individual differences in the tendencies to use particular modes of connectivity were related to cognitive control. Specifically, modes which showed strong modular networks and anticorrelated relationships from visual and somatosensory areas to cerebellar regions, were significantly correlated with improved performance on several executive tasks including measures of cognitive flexibility, processing speed, and working memory but not with fluid intelligence or inhibition and attention (Nomi et al., 2016).

As reviewed above, analyses of structural, functional, and connectivity relationships to cognitive control have often identified overlapping regions. For example, both the structural and functional activation meta-analyses point to lateral and medial regions of prefrontal cortex, as have some of the functional connectivity studies. However, what is not clear is whether these are the same regions of prefrontal cortex across modalities or studies, and whether they correlate across individuals. Further, how do patterns in large-scale network organization from rsfcMRI data in and between those regions relate to measures of cortical thickness and functional activation? How do these patterns across different imaging modalities relate with behavior? These questions are difficult to answer with single modality studies, and their answers could provide broader insights into neural functions.

1.2. Examining multiple modalities

Given the complementary strengths and weaknesses associated with each modality (Biessmann et al., 2011), many studies collect several different imaging modalities in the same individual, often in the same scanning session. However, many investigators choose to analyze these different imaging modalities using independent analysis pathways (Groves et al., 2011). With such an approach, the integration of findings occurs post-hoc using approaches such as correlation between measures or visual inspection and description (Groves et al., 2012; Calhoun and Sui, 2016). For example (Westlye et al., 2009), correlated the results of independently processed DTI data with EEG data from a flanker task which identified a significant relationship between the two modalities in the posterior left cingulum. Similarly (Harms et al., 2013), used a post-hoc correlation based approach and identified a relationship between volume of the superior and middle frontal gyri and working memory related activity in the intraparietal sulcus and a relationship between hippocampal volume and working memory related activity in the dorsal anterior cingulate and left inferior frontal gyrus (Harms et al., 2013).

While such correlational approaches are important and have yielded informative results, they represent a univariate approach to a multivariate problem (Calhoun and Sui, 2016). This can generate a unique set of findings within a given modality with relatively little guidance as to how the results fit together across modalities (Sui et al., 2012a,b; Pearlson et al., 2015; Calhoun and Sui, 2016). As shown in (Calhoun and Sui, 2016), data from (Plis et al., 2011) were used to perform independent analyses in fMRI and MEG data that were collected from the same set of subjects performing the same task. These data were used to generate network graph representations for both modalities independently and resulted in graphs with highly dissimilar structures and properties. In contrast, combined multimodal analysis using the same data led to brain networks in the individual modalities that were highly spatially correlated. While further data are needed to determine whether one type of analysis approach versus the other is better related to external validators, the findings do suggest the univariate approach to multimodal data analysis does not always identify coherent patterns across modalities.

1.3. Multimodal fusion analysis approaches

To address this, recent methodological advances have provided a new set of analysis tools aimed towards solving the difficulties in adjudicating between dissimilar results generated by analyzing multiple modalities in separate pathways (Michael et al., 2010; Biessmann et al., 2011; Groves et al., 2011; Sui et al., 2012a,b; Calhoun and Sui, 2016). These methods enable analysis of multiple imaging modalities in a single analysis, which allows for simultaneous study of the brain at multiple levels of analysis and capitalizes on the complementary strengths across modalities (Biessmann et al., 2011). Further, these approaches are able to identify joint variance structures that help us understand the shared patterns contained within the different modalities of data and can present a richer understanding of the neural constructs under examination (Sui et al., 2012a,b).

One such method is multiset canonical correlation analysis with joint independent component analysis (mCCA + jICA) (Sui et al., 2011; Sui et al., 2012a,b; Sui et al., 2013). This method simultaneously decomposes multiple modalities of data and identifies a set of hidden sources of variance that are linked across modalities and jointly contribute to the variation seen in the data. The combination of these two analysis methods, mCCA (Li et al., 2009) and jICA (Calhoun et al., 2006), overcomes the limitations of the individual methods (see (Sui et al., 2012a,b) for review) and provides a mathematical framework that enables the