NeuroImage 106 (2015) 144–153

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Effective connectivity within the frontoparietal control network differentiates cognitive control and working memory

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ARTICLE INFO

Article history:
Accepted 18 November 2014
Available online 22 November 2014

Keywords:
Cognitive control
Working memory
Dynamic causal modeling
Frontoparietal
Effective connectivity

ABSTRACT

Cognitive control and working memory rely upon a common fronto-parietal network that includes the inferior frontal junction (IFJ), dorsolateral prefrontal cortex (dlPFC), pre-supplementary motor area/dorsal anterior cingulate cortex (pSMA/dACC), and intraparietal sulcus (IPS). This network is able to flexibly adapt its function in response to changing behavioral goals, mediating a wide range of cognitive demands. Here we apply dynamic causal modeling to functional magnetic resonance imaging data to characterize task-related alterations in the strength of network interactions across distinct cognitive processes. Evidence in favor of task-related connectivity dynamics was accrued across a very large space of possible network structures. Cognitive control and working memory demands were manipulated using a factorial combination of the multi-source interference task and a verbal 2-back working memory task, respectively. Both were found to alter the sensitivity of the IFJ to perceptual information, and to increase IFJ-to-pSMA/dACC connectivity. In contrast, increased connectivity from the pSMA/dACC to the IPS, as well as from the dlPFC to the IFJ, was uniquely driven by cognitive control demands; a task-induced negative influence of the dlPFC on the pSMA/dACC was specific to working memory demands. These results reflect a system of both shared and unique context-dependent dynamics within the fronto-parietal network. Mechanisms supporting cognitive engagement, response selection, and action evaluation may be shared across cognitive domains, while dynamic updating of task and context representations within this network are potentially specific to changing demands on cognitive control.

Introduction

Cognitive control (CC) and working memory (WM) rely on neural processing within a common set of brain regions encompassing dorsomedial prefrontal, lateral prefrontal, and superior parietal regions of the human cortex (Fedorenko et al., 2013; Harding et al., in press; Niendam et al., 2012). This so-called "frontoparietal network" (FPN) represents a flexible, superordinate system supporting adaptive behavioral control across a broad range of cognitive demands (Cocchi et al., 2013; Cole et al., 2013; Dosenbach et al., 2008). The inherent flexibility of this system has been linked to rapid adjustments in neuronal response profiles as a function of changing behavioral goals or contextual cues (Kadohisa et al., 2013; Stokes et al., 2013). However, the neural mechanisms underlying such dynamic representation of unique behavioral goals and encoding of diverse contextual information remain unclear.

Functional neuroimaging research has established that activity in the regions forming the FPN demonstrate temporal coherence (i.e., functional connectivity) in human subjects at rest (Cole and Schneider, 2007; Power et al., 2011). The magnitude of these intrinsic inter-regional interactions has additionally been shown to selectively change in response to behavioral demands, as demonstrated most clearly in studies exploring the dynamic interplay between the dorsomedial and dorsolateral prefrontal cortices during cognitive control tasks (Carter and van Veen, 2007; Prado et al., 2011; Stephan et al., 2003).

More recently, research has moved beyond the study of FPN connectivity using pair-wise correlations in brain signals, employing techniques that are sensitive to network-wide and directional interdependencies (i.e., effective connectivity; Friston, 2011). Dynamic causal modeling (DCM) provides one means to infer neural interactions and their task-dependent changes within a brain network (Friston et al., 2003). In contrast to alternative effective connectivity modeling approaches (e.g., Structural Equation Modeling), DCM models dynamics at the level of neuronal populations, as opposed to the measured hemodynamics, providing greater construct validity to derived models of network function (Daunizeau et al., 2011). Moreover, DCM does not depend on the temporal precedence of one regional time series relative to another (as in

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http://dx.doi.org/10.1016/j.neuroimage.2014.11.039
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multivariate autoregressive models); reliance on temporal lag may be problematic to inference using fMRI data (Friston et al., 2013).

Studies employing DCM to explore the FPN have identified sparse task-related connectivity dynamics on top of a foundation of widespread task-invariant "baseline" interactions, largely mirroring correlation-based work (Cieslik et al., 2011; Fan et al., 2008; Schlosser et al., 2008; Wang et al., 2010). In particular, Schlosser et al. (2010) report modulations of medial–lateral prefrontal interactions during performance of a Stroop task, while WM load has been associated with the transient gating of, primarily, fronto-parietal connectivity (Deserno et al., 2012; Dima et al., 2014; Ma et al., 2012; Schmidt et al., 2014). These findings point to a well-integrated network whose interactions are selectively weighted in response to current behavioral demands, reflecting a potential mechanism of adaptive coding within the FPN (Duncan, 2001). However, dissimilar experimental protocols and definitions of the FPN across available investigations preclude a more unified account of the response of this network across different cognitive domains.

Here we utilize DCM to investigate task-related changes in the FPN as CC and WM demands are systematically co-varied within a single fMRI task. Task-related dynamics of the interactions between the visual system and the FPN are first explored to assess the shared versus unique mechanisms underlying the selective engagement of higher-order cognitive processes. Context-dependent plasticity between the major regions of the FPN as a function of CC or WM demands is then assessed to distinguish their relative contributions to underlying connectivity dynamics.

Materials & methods

Participants

Twenty-five right-handed healthy adults (14 males; mean age ± s.d. = 25.5 ± 4.4 years) with no history of psychiatric or neurologic illness were recruited from the general community through advertisements in local electronic media. Exclusion criteria included a history of psychiatric or neurologic illness, substance dependence, significant head injury, current use of psychotropic medications, or MRI incompatibility (e.g., cardiac pace-maker), as assessed using the Structured Clinical Interview for DSM-IV Axis-I Disorders (First et al., 2002) and self-report. Participants had completed an average of 14.8 ± 2.2 years of education and had a mean estimated full-scale IQ of 110 ± 10 (Wechsler Abbreviated Scale of Intelligence; Wechsler, 1999). This participant sample is the same as that reported in Harding et al. (in press). The local research and ethics committee approved study conduct and all participants provided written informed consent.

Behavioral paradigm

CC and WM demands were respectively manipulated using the multi-source interference task (MSIT; Bush and Shin, 2006) and a verbal *n*-back working memory task ($n = 0, 1$, or 2; Baddeley, 2003), combined in a 2 × 3 factorial design. This design allowed for orthogonal manipulation of CC and WM demands within a common task context. As illustrated in Fig. 1, and described in full detail elsewhere (Harding et al., in press), participants were presented with sets of three numbers ranging in value from '0' to '3', with one number distinct to the other two (e.g., '2 1 1'), and instructed to identify the distinct number by button press ('1' = index; '2' = middle; '3' = ring fingers). CC demands were manipulated by altering the composition of the number-sets: "congruent" trials featured the distinct number paired with zeros, which do not represent a response alternative, and spatially aligned with the corresponding response finger; conversely, "incongruent" trials featured both 'Flanker' interference introduced by distracter numbers (Eriksen and Eriksen, 1974) and 'Simon' conflict based on spatial incongruence between the target digit and the corresponding response finger (Simon and Berbaum, 1990). Working memory demands were introduced by requiring participants to withhold a response if the current 'distinct' number was the same as that presented '*n*' trials previously (where *n* represents the working memory load: 1 or 2). Two trials in which this condition was met were included in each working memory block.

The six conditions were presented in alternating blocks containing 8, 9, or 10 stimuli for 0-Back, 1-Back, and 2-Back blocks, respectively. The first stimulus in 1-Back blocks, and first two in 2-Back blocks were discarded during analysis to account for 'ramping-up' of WM load. Each stimulus was presented for 2 s and separated by variable interstimulus intervals of between 3.6 s and 7.2 s. Four blocks of each condition were presented across the experiment, each preceded by an instruction screen indicating the *n* of the subsequent block.

fMRI data acquisition

Images were obtained on a 3-Tesla Siemens Trio scanner equipped with a 32-channel head coil. Each functional run consisted of 354 whole-brain gradient-echo echo-planar (GRE-EPI) images composed of 36 interleaved, contiguous axial slices (TR = 2400 ms; TE = 32 ms; flip angle = 90°; slice thickness = 3 mm; in-plane resolution (matrix) = 3.3 × 3.3 mm (64 × 64); FOV = 210 × 210 mm). A high-resolution T1-weighted MPRAGE structural image was also acquired (176 sagittal slices; 0.9 mm isotropic voxels; TR = 1900 ms; TE = 2.24 ms; FOV = 230 × 230 mm; matrix = 256 × 256).

fMRI data analysis

Analysis was performed using SPM8 software (Functional Imaging Laboratory, UCL, UK). Structural (T1-weighted) images from each individual were first coregistered to the functional data and normalized to standard space (DARTEL; Ashburner, 2007). The estimated nonlinear transformation parameters were subsequently applied to the (rigid-body) motion-corrected functional data. The normalized data were interpolated to 2 mm isotropic voxels and spatially smoothed using a Gaussian kernel of 8 mm FWHM.

For each individual, the six task conditions were coded as individual predictors in a general linear model, alongside nuisance regressors accounting for error trials, instruction periods, and working memory ramping effects (i.e., first trial in 1-back blocks and first two trials in 2-back blocks). Each stimulus event was coded as a delta (i.e., stick) function and convolved with a canonical hemodynamic response function. Data were high-pass filtered (1/128 s), and temporal autocorrelations were estimated using a first-order autoregression model [AR(1)]. Parameters corresponding to each predictor were estimated using a restricted maximum likelihood approach. Contrast images were created among the six conditions of interest to infer the main positive effects of CC and WM (voxel-level family-wise error corrected $p < 0.05$) within a repeated-measures ANOVA framework.

Dynamic causal modeling

Deterministic, bilinear dynamic causal models (Friston et al., 2003) were used to assess large-scale neural interdependencies within the FPN using differential state equations comprised of three sets/matrices of parameters: A, context-invariant intrinsic influences between regions; B, context-dependent modulations of the intrinsic connections as a function of CC and WM demands; and C, exogenous visual inputs. Models of neuronal dynamics were combined with a hemodynamic model that describes the relationship between the (hidden) neuronal activity of the system and the measured fMRI signal (Friston et al., 2000). The parameters of the integrated model were estimated using a Bayesian inversion algorithm (Friston et al., 2003), as implemented in the DCM10 toolbox (Functional Imaging Laboratory, UCL, UK).

We tested a broad variety of models (see below). Estimates of the posterior evidence of these models were derived during Bayesian