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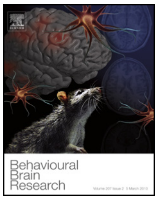

Research report

The dorsal prefrontal and dorsal anterior cingulate cortices exert complementary network signatures during encoding and retrieval in associative memory

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HIGHLIGHTS

- Cognitive control is important for associative memory processes.
- Dorsal anterior cingulate (dACC) and dorsal prefrontal cortices (dPFC) are implicated.
- dACC and dPFC exert differentiable cognitive control during memory processes.
- dACC and dPFC exert complementary control on hippocampus during memory processes.
- Learning rate correlated with degree of preferential seed-target modulation.

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ABSTRACT

Cognitive control includes processes that facilitate execution of effortful cognitive tasks, including associative memory. Regions implicated in cognitive control during associative memory include the dorsal prefrontal (dPFC) and dorsal anterior cingulate cortex (dACC). Here we investigated the relative degrees of network-related interactions originating in the dPFC and dACC during oscillating phases of associative memory: encoding and cued retrieval. Volunteers completed an established object-location associative memory paradigm during fMRI. Psychophysiological interactions modeled modulatory network interactions from the dPFC and dACC during memory encoding and retrieval. Results were evaluated in second level analyses of variance with seed region and memory process as factors. Each seed exerted differentiable modulatory effects during encoding and retrieval. The dACC exhibited greater modulation (than the dPFC) on the fusiform and parahippocampal gyrus during encoding, while the dPFC exhibited greater modulation (than the dACC) on the fusiform, hippocampus, dPFC and basal ganglia. During retrieval, the dPFC exhibited greater modulation (than the dACC) on the parahippocampal gyrus, hippocampus, superior parietal lobule, and dPFC. The most notable finding was a seed by process interaction indicating that the dACC and the dPFC exerted complementary modulatory control on the hippocampus during each of the associative memory processes. These results provide evidence for differentiable, yet complementary, control-related modulation by the dACC and dPFC, while establishing the primacy of dPFC in exerting network control during both associative memory phases. Our approach and findings are relevant for understanding basic processes in human memory and psychiatric disorders that impact associative memory-related networks.

1. Introduction

Cognitive control is an important meta-cognitive construct encompassing a range of multidimensional processes that facilitate the execution of effortful, goal-directed cognitive tasks [1]. Cognitive control mechanisms extend across multiple cortical regions [2], and mediate processes including attentional control, selection and extraction of process-relevant information, and context-dependent

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cognitive process switching [1]. Context-dependent switching is particularly relevant to cognitive control as many tasks oscillate between complementary psychological processes that may engage distinct control-related demand. Two regions of the frontal lobe are implicated in executive processes: the dorsal anterior cingulate (dACC) and the dorsal prefrontal cortex (dPFC) [3–7]. Prior functional magnetic resonance imaging (fMRI) studies have highlighted the relative specialization of these regions using tasks that require varying degrees of cognitive control. Here we extend those studies by investigating the modulatory influence of each of the dPFC and the dACC on cortical and sub-cortical targets during two complementary processes of associative memory. Specifically, we focused on assessing whether the dPFC and dACC exerted spatially-distributed modulation on target brain regions during the encoding and retrieval of object-location associations.

Memory encoding involves the pairing of distinct, often novel memoranda, such that either memoranda and/or their association can be voluntarily recalled in the future [8,9]. Effective memory encoding is dependent on several specialized regions distributed across the frontal-hippocampal network [8–12]. Germane to this investigation, the object-location association network included a diverse network of regions including the dACC, the dPFC, the parahippocampal gyrus (PHG), the fusiform gyrus, the parietal lobe, basal ganglia, and the hippocampus. The PHG is associated with spatial processing (i.e. object location) while the fusiform is associated with object recognition [8,12–14]. The basal ganglia is interconnected with the PFC and may be involved in ‘gating’ information maintained in the dPFC or object-location rehearsal during memory encoding [1,15,16]. The hippocampus is critical for the binding of memoranda (i.e. an object with its spatial location) [8,12]. Published data motivated the present investigation of the relative contributions of the two seed regions: dACC and dPFC. Evidence implicates the dACC in control of memory-relevant attention, information filtering and extraction, and conflict monitoring [1]. Specific to object–location associative memory, the dACC is hypothesized to monitor performance, ignore task-irrelevant distractions (e.g. irrelevant object-related memories or environmental stimuli, such as scanner noise), and block conflicting or competing incorrect object–location associations [1,7,8,16]. Previous fMRI studies demonstrated the dACC is active during both encoding and recognition/retrieval of associative memories [8]. However, to our knowledge, no studies have specifically assessed network profiles of the dACC during associative memory.

The dPFC sub-serves the selection and active mental representation of the memoranda to be paired during encoding [11,17]. Extensive evidence implicates the dPFC’s involvement in active mental representations of memoranda during brief delay periods (i.e. working memory) [17–21]. Moreover, several studies demonstrated the dPFC’s involvement in active mental representation and organization of memoranda prior to associative memory encoding (for review see [11]). Recent work demonstrated directed interactions between the hippocampus and other constituent regions during encoding [22]. Memory binding is a process initiated by the hippocampus and consolidated through cortical–hippocampal interactions, yet, few studies have assessed directed top-down control of memory binding.

Cued memory retrieval also relies on cognitive control and processing within the memory network (which implicates many of the same brain regions as encoding) [8,12]. In this study, the cue is a spatial location on a fixed three by three grid which implicates the involvement of the superior parietal lobule (SPL) and the PHG [8,12]. fMRI studies indicate an important role for the PFC in executing top-down cognitive control of these regions to facilitate accurate memory retrieval. Miller and D’Esposito demonstrated phase coherence between the PFC and the hippocampus (PFC activity preceded hippocampal activity) during memory recognition [8]. However, little is known about the unique and potentially complementary role of sub-regions within the PFC (e.g. dPFC and dACC) during these control processes.

Recent work suggested that the mechanisms of action of the dPFC and the dACC occur via amplification of sub-cortical and cortical responses in process-relevant regions [23–25]. By implication, efferent signals from frontal structures may enhance cortical and sub-cortical responses during cognitive control as has been previously shown in the context of working memory [24,25]. Such evidence elaborates the putative network roles of the dACC and the dPFC: these structures are not merely specialized for processing conflict or control during tasks, but through modulation of brain networks, engage in the functional integration of control-related processing in complex cognitive tasks. The current study extends this idea and examines process-specific roles during a frontal–hippocampal associative memory paradigm [11].

1.1. Aims and hypotheses

Using a variant of a widely-employed associative memory paradigm [26], we compared the modulatory effects [27] of the dPFC and the dACC (relative to each other) across an *a priori* cortical–striatal network during memory encoding and cued retrieval. The analytic approach, psychophysiological interaction (PPI), was selected to model our *a priori* hypotheses of distinct, and yet potentially complementary, seed-to-target effects. This analytic approach provided a robust and well-characterized linear model to assess this pattern of inter-regional and directional connectivity from fMRI signals [27–29]. In addition, we also conducted exploratory analyses to link behavioral proficiency (i.e., learning rate across associative memory epochs) and the relative degree of control-related modulation of the hippocampus by the dACC (>dPFC) and dPFC (>dACC) during encoding and/or retrieval. This exploration is motivated by the idea that control mechanisms act to facilitate performance (via functional integration) during relatively complex cognitive tasks.

2. Methods

2.1. Participant recruitment

All experimental procedures were approved by the Wayne State University Institutional Review Board. Participants provided informed consent prior to their involvement and received monetary compensation for participation. Enrolled participants ($N = 10$) were free of psychiatric or neurological conditions, with an average age of 22 years (range: 18–29 years; 5 females).

2.2. Imaging parameters

Gradient echo fMRI signals were acquired on a 4 T system (Bruker MedSpec) using an 8 channel head coil (TR = 3 s, TA = 2 s, TE = 30 ms, matrix = 64×64, slices = 24, FOV = 240 mm, voxel size = $3.75 \times 3.75 \times 4.0$ mm, images = 288). During the scan, stimuli were projected from a computer onto a screen mounted over the participant’s head. Head motion was restricted using foam inserts surrounding the participant’s head and earplugs were provided to reduce scanner noise.

2.3. Experimental design

During fMRI, all participants completed the object–location associative memory paradigm. The paradigm (Fig. 1) consisted of eight memory blocks cleaved into encoding and retrieval epochs [26]. During encoding, illustrations of nine common mono-syllabic