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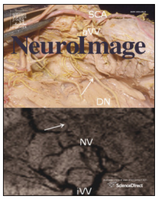

Context-specific differences in fronto-parieto-occipital effective connectivity during short-term memory maintenance

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ABSTRACT

Although visual short-term memory (VSTM) performance has been hypothesized to rely on two distinct mechanisms, capacity and filtering, the two have not been dissociated using network-level causality measures. Here, we hypothesized that behavioral tasks challenging capacity or distraction filtering would both engage a common network of areas, namely dorsolateral prefrontal cortex (dlPFC), superior parietal lobule (SPL), and occipital cortex, but would do so according to dissociable patterns of effective connectivity. We tested this by estimating directed connectivity between areas using conditional Granger causality (cGC). Consistent with our prediction, the results indicated that increasing mnemonic load (capacity) increased the top-down drive from dlPFC to SPL, and cGC in the alpha (8–14 Hz) frequency range was a predominant component of this effect. The presence of distraction during encoding (filtering), in contrast, was associated with increased top-down drive from dlPFC to occipital cortices directly and from SPL to occipital cortices directly, in both cases in the beta (15–25 Hz) range. Thus, although a common anatomical network may serve VSTM in different contexts, it does so via specific functions that are carried out within distinct, dynamically configured frequency channels.

Introduction

A growing body of evidence suggests that visual short-term memory (VSTM), and the related construct of working memory, may share common neural bases with selective attention (e.g. Nobre and Stokes, 2011; D'Esposito and Postle, 2015). In the domain of spatial cognition, for example, both engage a highly overlapping network of frontoparietal regions (e.g., Ikkai and Curtis, 2011), from which information can be "read out", depending on context, to accomplish oculomotor, attentional, or mnemonic goals (Jerde et al., 2012). Additionally, training on a visual working memory task has comparable effects on event-related potential (ERP) components associated with VSTM (the contralateral delay activity; CDA) and with visual selective attention (the contralateral search activity (CSA)) (Kundu et al., 2013), suggesting that there is a relationship between the underlying mechanisms supporting VSTM and visual selective attention. The CDA is an ERP component derived during a VSTM task, for which the amplitude scales monotonically with the number of items being held in VSTM, and plateaus at an individual's VSTM capacity (Vogel and Machizawa, 2004). The CSA is an ERP component derived during visual search for which the amplitude correlates with individual differences in VSTM capacity (Emrich et al., 2010).

One influential model of attentional control, operationalized through the Attentional Network Task, is organized into three dissociable components: alerting, orienting, and executive control (Fan et al., 2002). Machizawa and Driver (2011) related this framework to working memory by applying a principal components analysis to a behavioral dataset, and found that not only did putative measures of alerting, orienting, and executive control load independently onto the first three principle components, but so too did measures relating to three constructs from VSTM: capacity, precision, and filtering, respectively. In this paper we focus on the constructs of capacity and filtering. The former, in particular, has been of interest due to its ability to predict individual variation in cognitive measures such as search efficiency (Emrich et al., 2010) and filtering efficiency (Vogel et al., 2005), as well as higher-order measures such as educational achievement (Cowan et al., 2005; c.f. Cusack et al., 2009). Although capacity and filtering have both been related to the CDA (Vogel and Machizawa,

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Abbreviations: STM, short-term memory; EEG, electroencephalogram; VSTM, visual short-term memory; ERP, event-related potential; CDA, contralateral delay activity; CSA, contralateral search activity; TMS, transcranial magnetic stimulation; dlPFC, dorsolateral prefrontal cortex; SPL, superior parietal lobule; cGC, conditional Granger causality; TD, target-epoch distraction; ITI, intertrial interval; BEM, boundary-element model; EM, expectation-maximization; MVAR, multivariate autoregressive; ICA, independent components analysis.

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2004; Vogel et al., 2005), the two have not, to our knowledge, been dissociated at the network level. The goal of this study, therefore, was to interrogate the dorsal frontoparietal network with a method capable of detecting context-dependent differences in its EEG dynamics.

Specifically, we tested whether there is evidence of systematic differences in effective connectivity within a network comprising dorsolateral prefrontal cortex (dlPFC), superior parietal cortex (SPL), and extrastriate cortex during the delay-period of a VSTM task that emphasized either capacity or filtering. The rationale for choosing these areas lies in the findings from Kundu et al. (2013) which showed that working-memory training increases transcranial magnetic stimulation (TMS)-based measures of effective connectivity between dlPFC and SPL, as well as between SPL and extrastriate visual areas. It also showed that connectivity between dlPFC and SPL increases with VSTM load. Importantly, single pulse TMS provides a measure of effective connectivity such that we know exactly where and when stimulation occurred and thus we can measure its downstream effects in time through a data-driven manner (Casali et al., 2010). However, this method is limited in that it can only address the relative differences in connection strengths between the area stimulated and other distal areas. It cannot probe a predetermined connection between any two regions. Thus, the present study builds on the network model implicated by Kundu et al. (2013), but tests the hypothesis that different task contexts will be associated with systematic variation in the strength and direction of connectivity within the network.

This was accomplished using high-density (EEG) data and a recently developed method (Cheung et al., 2010) to estimate the conditional Granger causality (cGC) metric (Bressler and Seth, 2011) between dlPFC, SPL, and occipital cortex. Thus this method measures effective connectivity in its simplest sense, which is the change in electrical activity at one location as a weighted sum of changes elsewhere (Friston, 1994; and as explicated by us previously in Dentico et al. (2014) and Piantoni et al. (2013)). We do note, however, that the term 'effective connectivity' has also been used to refer more specifically to causal interactions measured in neurobiologically based models, such as dynamic causal modeling (see Friston, 2011 for a review). Such measures of effective connectivity can address the precise chronometry between networks that act as candidate sources of top-down control (Miller and D'Esposito, 2005). We hypothesized that increases in memory load and increases in filtering demands would produce differences in the strength and/or direction of effective connectivity between dlPFC and SPL, as well as between these areas and extrastriate occipital cortex, depending on context.

Methods

Participants

Data reported in the present study were taken from the pre-training session of a working memory training study (Kundu et al., 2013). 30 participants (16 female, mean age = 20.9 years, *SD* = 2.75 years) were recruited for the study from the University of Wisconsin-Madison community. The inclusion criteria selected healthy participants between the ages of 18–35 years, with normal or corrected-to-normal visual acuity and normal color vision, and who were not currently taking medication for psychiatric conditions. All procedures were approved by the University of Wisconsin-Madison Institutional Review Board.

Overview of tasks

Two tasks were used to test short-term memory (STM). The location VSTM and Target-epoch distraction (TD) tasks were selected because they operationalize two theoretical factors — capacity and filtering, — hypothesized to account for individual differences in STM and selective attention (Machizawa and Driver, 2011). Each subject performed the location VSTM task and then the TD task.

Location VSTM task

The trial began with a cue indicating the visual hemifield that was relevant for that trial. Then, either two (Load 2) or four (Load 4) black squares ("target stimuli") were presented serially in the cued hemifield, along with a comparable, simultaneous sequence in the uncued hemifield ("foil stimuli"). Load condition varied randomly (without replacement) on a trial-by-trial basis, as did the location of each target and foil, which was determined by using a random number generator to generate coordinates within a predetermined area of the visual field. Then there was a delay period of 3750 ms after which a probe that either did or did not match ($P = 0.5$) the location of one of the stimuli appeared (Fig. 1A). Subjects were instructed to maintain central fixation throughout the delay. The subjects indicated whether the probe matched the location of any one of the memory targets presented in the cued hemifield via left/right button press at the end of the trial. Subjects used both of their hands, right thumb for the right button and left thumb for the left button. Left and right button assignments indicated match and non-match responses respectively. These button assignments were the same across subjects (i.e. button assignment was not counterbalanced). Note, counterbalancing was not required because the analyses were restricted to the delay period, when no responses were being made, and when subjects could not predict what the response would be. The probe always appeared in the cued hemifield. Feedback was provided on a trial-by-trial basis, with the word "Incorrect" appearing on the screen for 500 ms following an incorrect response. The intertrial interval (ITI) was 550 ms. The task block consisted of 480 trials presented in sub-blocks of 60 trials. Two transcranial magnetic stimulation (TMS) pulses were delivered during the delay period of 50% of the trials, selected at random. The data from the TMS-present trials will not be discussed in this report. The participants received verbal instructions and completed a block of trials prior to testing. The practice blocks were repeated until a criterion of 75% accuracy was reached. No more than three practice blocks were required for any subject. Memory targets were presented within a 4.3° × 8.6° region in hemifield, centered ~3.3° horizontally from fixation. Memory targets consisted of black squares subtending ~1° of visual angle at a viewing distance of 70 cm and were presented on a gray background. The probe consisted of a black square (~1° of visual angle). The probe for non-match trials was presented at a

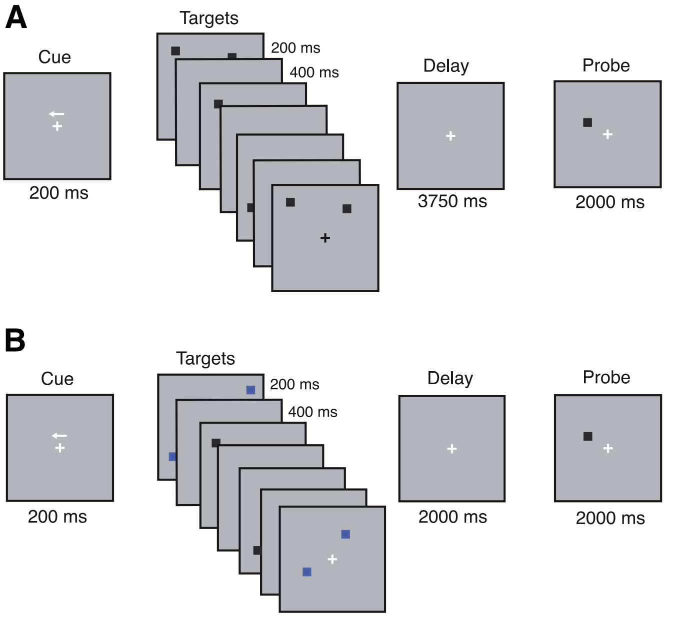

Fig. 1. Schematic representation of tasks. (A) Location VSTM task. Example of a *Load 4* trial. Memory targets ("targets" in the figure) were black, as was the probe. (B) Target-distraction (TD) task. Example of a *Load 2d* trial. In this task relevant stimuli were presented in black and irrelevant stimuli in blue.

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