# Effects of Interference in Working Memory on Prefrontal Cortex Activity: A Test of a Computational Model

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## Introduction

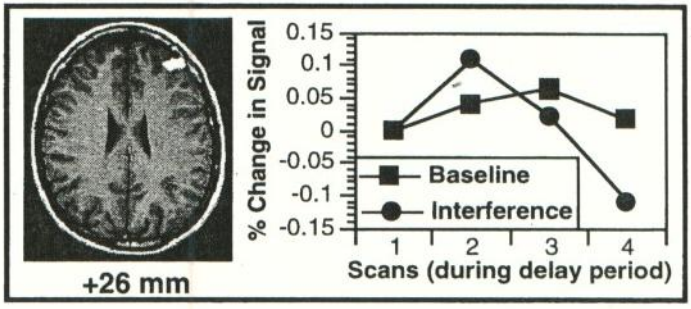
We have suggested that the prefrontal cortex (PFC) plays a critical role in working memory (WM) by actively maintaining prior context information to mediate appropriate behavioral responding (1). We have provided support for this hypothesis in previous neuroimaging studies, by showing that PFC activity increases with both memory load (2) and delay (3), and is sustained throughout the entire delay period (3,4). Recent computational modeling work has suggested an additional, strong prediction of this hypothesis: That manipulations which interfere with active maintenance of context should produce decay in PFC activity during the retention interval (5). In the current study, we tested this prediction by examining PFC under both baseline and interference conditions of a WM task.

## Methods

Twenty subjects performed a variant of the AX-CPT task that was used successfully in a previous study to elicit PFC activity through manipulations of delay (3). Performance requires maintenance of cue information over the delay period in order to respond appropriately to an ambiguous probe. Trials lasted 20 sec, and included a cue (0.5s), a delay period (retention interval; 9.5s), a probe (0.5s), and an intertrial interval (ITI; 9.5s). Stimuli were single letters presented centrally on a visual display. In the interference condition, irrelevant letters (appearing in a different color) were presented at a regular rate during both the delay period and ITI. This manipulation has been observed in previous behavioral experiments to produce a performance signature that is clearly indicative of a disturbance in the active maintenance of context (5). Subjects performed 80 trials of each condition, in blocks of 10 trials each (3.5 min duration). Eight scans were acquired during each trial at 16 axial locations ($3.75mm^3$). Scans were synchronized to the start of the trial and were acquired using a 2-interleave spiral-scan pulse sequence (TR = 1250ms, TE = 35ms, FOV = 24cm, flip=60°) on a 1.5T GE Signa scanner. The functional imaging data were movement corrected, co-registered, smoothed (using an 8mm FWHM Gaussian filter), and pooled across subjects in a procedure described previously (2,3,4). Data were analyzed through an ANOVA with task (baseline vs. interference) and scan (scans 1-8) as factors. Two sets of analyses were conducted: confirmatory, using ROIs derived from our previous study using this task (3); and exploratory, using a voxelwise approach, and examining the entire dataset.

## Results

The primary effect of interest was the presence of a task x scan interaction. This effect was found (p=.05) in the confirmatory analysis on the left dorsolateral PFC ROI (BA 46/9; see Figure). Delay-related activity in this region decayed more quickly in the interference condition compared to baseline. Interestingly, however, the peak amplitude of activity was greater under interference. The exploratory analysis revealed an additional region in right dorsolateral PFC (BA 9), that also showed decay of delay-related activity under interference. Thus, the results confirm the prediction of the model, and provide support for the hypothesis that PFC activity is causally related to the active maintenance of context in WM.




## References

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