Cortical Representation of Multiple Visual Stimuli in Working Memory

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Abstract of the Dissertation
Cortical Representation of Multiple Visual Stimuli in Working Memory
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It has been suggested that interference between items is an important factor limiting the working memory capacity. Neuroimaging studies have shown increases in activity in the prefrontal cortex (PFC) and posterior parietal cortex (PPC) with increasing number of to-be-remembered items. This dissertation is to examine whether items from different categories (cross-category) are better recognized than those from the same category (within-category) and whether multiple items are equally represented in the PFC and PPC. Behavioral data were collected from 50 participants while they performed various versions of a delayed recognition task in 3 experiments and functional magnetic resonance imaging (fMRI) data were collected from 16 participants. The task required participants to memorize two visual stimuli either from the same or different categories (color, bar orientation or shape). Behavioral results showed that recognition performance is better for the cross-category condition compared to the within-category condition and results from a control experiment suggested that perceptual competition is not the main source of the behavioral difference. In addition, the second item has a greater effect on the recognition of the first item than the opposite. FMRI results showed that the bilateral intraparietal sulcus (IPS), superior parietal lobe (SPL) and left dorsal PFC are more active during remembering orientations than colors. The left ventral posterior IPS and pre-central sulcus (PrCS) showed stronger responses during retention of two items than that of one item regardless of feature. The right pre-central sulcus (PrCS) showed greater responses to remembering two orientations than remembering one item or two items from different categories. The right dorsal PFC and IPS showed a larger increment in activation when remembering two orientations than when remembering two items from different categories. In sum, these findings show that competition between remembering two items of the same category dampens recognition performance, suggesting larger interference between items from the same category. The right dorsal PFC and PPC may be involved in representing items share similar features.

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Abbreviations

DLPFC	dorso-lateral prefrontal cortex
FEF	frontal eye field
FFA	fusiform area
IFG	inferior frontal gyrus
IT	inferior temporal cortex
LG	lingual gyrus
IPL	inferior parietal lobe
IPS	intraparietal sulcus
ITG	inferior temporal gyrus
LOC	lateral occipital cortex
MFG	middle frontal gyrus
MTG	middle temporal gyrus
Pcu	precuneus
PFC	prefrontal cortex
PM	premotor
PPA	parahippocampal area
PPC	posterior parietal cortex
PrCG	precentral gyrus
preSMA	pre-supplementary motor area
SFS	superior frontal sulcus
SMA	supplementary motor area
SPL	superior parietal lobe
VLPFC	ventro-lateral prefrontal cortex

ERP	event related potential
fMRI	functional magnetic resonance imaging
ISI	interstimulus interval
ROI	region of interest
rTMS	repetitive transcranial magnetic stimulation

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1. Background

1.1 What is capacity of working memory?

Working memory capacity has been defined as the number of items that can be held in memory for a short period of time (Cowan, 2001) and has been studied by many researchers (Alvarez & Cavanagh, 2004; Eng, Chen, & Jiang, 2005; Luck & Vogel, 1997; Vogel, Woodman, & Luck, 2001; Xu & Chun, 2006). The capacity of working memory is extremely limited and performance is affected by many factors. In previous studies, researchers have investigated the effects of sequential presentation, stimulus complexity and distraction on working memory performance. However, it is still not clear how well individual items are represented and how items interfere with each other in working memory. The purpose of this study is to provide behavioral and neuroimaging data on visual information processing in multiple item working memory tasks.

1.2 Behavioral measures of the encoding and maintenance of multiple items in visual working memory

When there are multiple items to remember, memory performance for the intermediate items is worse than for the first item and the most recent item. The first item produces better recognition accuracy than the intermediate items (Golob & Starr, 2004; McElree & Dosher, 1989). Increasing the interval between memory items does not change the memory performance, while increasing the number of items between the remembered item and testing item decreases the performance (Waugh & Norman, 1965). Other studies have shown that adding distractors before retrieval disrupts memory performance as well (Brown & Brown, 1958; Peterson & Peterson, 1959). These behavioral studies suggested that interference between items decreases memory for intermediate items.

Recent studies are also consistent with the notion that memory performance is best for the most recent display (Jiang, 2004; Jiang & Kumar, 2004; Kumar & Jiang, 2005). They showed that as the interval increases (within 200ms), memory performance for the first display dropped. They suggested it was due to the second item disrupting the consolidation of the first display. While as interval increased to 500ms or more, the performance of the first display increased but still worse than the second display. It could be due to the second display interfered with the first display in working memory (Jiang, 2004; Jiang & Kumar, 2004; Kumar & Jiang, 2005). Such findings are consistent with eye movement studies, which have found higher recognition accuracy for the most recently fixated stimulus (Zelinsky & Loschky, 2005). However, at very shorter intervals (< 50ms), the recognition rate for the first display is as good as for the second display, suggesting that the two displays are integrated together (Jiang, 2004; Jiang & Kumar, 2004; Kumar & Jiang, 2005). It has been shown in a more recent study that a visual working memory can be consolidated within 200ms (Vogel, Woodman, & Luck, 2006). The consolidation time suggested by Jiang et al was longer (200-500ms) than what Vogel et al have found. As Vogel et al (2006) presented all memory stimuli in one display and the participant did not need to remember the distractors presented afterwards, while Jiang and her colleague used sequential display, and the participants had to remember the second display as well as the first display. Thus, encoding new target items might have a greater effect on consolidation of the first display.

In summary, visual working memory has limited capacity. Interference appears to play an important role in working memory and it is a key issue in understanding the limitations of working memory. It has been shown that the recognition of different items in a sequential presentation is not equal. The extent of interference between individual items in working memory needs to be further investigated. The current study examined the interference between items in working memory. In the next part, we discussed the interference between items as a basis of performance deterioration in working memory tasks.

1.3 Interference between items – neuroimaging findings

Interference has been defined as "mutual degradation of memory traces that are held in working memory simultaneously" (Oberauer & Kliegl, 2001, pg. 190). The limited capacity of working memory has been suggested to be caused by interference between items (Oberauer & Kliegl, 2001, 2006; Oberauer & Lewandowsky, 2008). In Oberauer and his colleagues' interference model, they assume that each item is represented by a number of features. When multiple items are maintained in working memory, any two items sharing the feature may compete and one item may lose the representation of that feature (Oberauer & Kliegl, 2006).

When stimuli are presented sequentially, the interference can occur in at least two ways: (1) holding an item in working memory may reduce the capacity for encoding new items; and (2) remembering a new item may affect the maintenance of existing items in working memory. According to the interference model, interference is expected to be less for items from different categories than from the same category. We expect to see higher accuracy and shorter response time on the items from different categories than from the same categories.

1.3.1 Interference within the same category vs. across different categories

Behavioral experiments have shown that an item that has multiple features from different dimensions has higher recognition rate than multiple features from the same dimension (Kumar & Jiang, 2005; Olson & Jiang, 2002; Wheeler & Treisman, 2002). Jiang and colleagues presented stimuli in two displays in a working memory task. They found that displays of stimuli from different categories showed higher recognition rate than displays of stimuli from the same category (Kumar, & Jiang, 2005). Inserting a secondary task during the delay period had a greater impact on working memory performance when both tasks used stimuli from the same domain than from different domains. And it was tested between spatial location and visual pattern (Della Sala, Gray, Baddeley, Allamano, & Wilson, 1999), spatial location and color (Vuontela, Rama, Raninen, Aronen, & Carlson, 1999) and visual pattern and verbal material (Logie, Zucco, & Baddeley, 1990). There was less interference between color and orientation information than orientation and distance information (Mohr & Linden, 2005). In sum, in working memory tasks, information from different categories demonstrated less interference than information from the same category.

1.3.2 Effect of working memory load on subsequence information processing

Previous studies revealed that additional cognitive demands altered the perceptual processing of task-irrelevant information (Lavie & Tsal, 1994; Lavie, 1995). Lavie and her colleagues suggested that high working memory load decreased the ability to inhibit task-irrelevant information (Lavie, Hirst, de Fockert, & Viding, 2004). The task-irrelevant information caused larger intrusion under high working memory load than under low working memory load condition in a Stroop-like task (de Fockert, Rees, Frith, & Lavie, 2001), a flanker task (Lavie et al., 2004) and a visual search task (Lavie & de Fockert, 2005). In de Fockert et al's study (2001), participants had to make a judgment with respect to a name superimposed on a face. The face could be either congruent with the name or incongruent. The participants had to remember a list of digits before each trial. In the high working memory load condition, the digits were random numbers. In the low working memory load condition, the digits were in sequential order. In the high working memory load condition greater activations in were observed in brain regions associated with face perception and processing including the fusiform area (FFA) and inferior occipital and lingual gyri (Kanwisher, McDermott, & Chun, 1997). This could have been due to the fact that in the high working memory load condition there was less remaining capacity to suppress the task relevant information from distraction.

Different from Lavie et al's findings, other studies have found that increased working memory load reduced perceptual processing of task-irrelevant information (Klemen, Büchel, Bühler, Menz, & Rose, in press; Rose, Schmid, Winzen, Sommer, & Büchel, 2005; Sreenivasan, & Jha, 2007). In Rose et al's study, participants performed a visual object n-back task while event related potentials (ERP) and functional magnetic resonance imaging (fMRI) were collected. The amplitude of N1 (150ms-200ms after the onset of the stimulus), and activity in the lateral occipital cortex, increased as the visibility of the visual images increased. However, the increment was reduced under high demand of working memory load. Since N1 and the lateral occipital cortex (LOC) are associated with perception of visual information (Hillyard & Anllo-Vento, 1998; Luck & Hillyard, 1995; Malach et al., 1995), the results indicate that visual processing was reduced under high working memory load (Rose et al., 2005). Moreover, the reduction was also dependent on the category of the distractor and the information held in working memory. The N170 component, which was found to be sensitive to face perception (Bentin et al., 1996), was reduced more in response to a face distractor during face working memory than in non-face working memory (Sreenivasan, & Jha, 2007). Klemen et al suggested the differences between theirs and Lavie et al's could be due to the task discrepancy. The working memory load reduced the ability in selective attention in early studies (de Fockert et al., 2001; Lavie et al., 2004) so that the interference from task-irrelevant information was larger. In the more recent studies, working memory load directly affected the processing of the visual distractor so that the N1 and the LOC activation was reduced under high working memory load condition (Klemen et al., in press; Rose et al., 2005).

These studies suggest that perceptual processing of a new item would be reduced in quality following an item from the same category than following an item from a different category.

1.3.3 Effect of processing new information on existing memory

Brain imaging studies have shown that the lateral PFC is involved in resisting interference during memory maintenance (Chao et al., 1995, 1998). In those studies, working memory was disrupted by task-irrelevant tones during the delay period for patients with the lateral PFC lesions. In addition, performance was most disrupted when the distractor task involved information processing in the same category as the remembered stimuli (Jha, Fabian, & Aguirre, 2004; Yoon et al., 2006; Screenivasan & Jha, 2007). In Yoon et al's study, when the task-relevant information and task-irrelevant information were in the same category, the activity of the DLPFC was lower than when they were in different categories (Yoon et al., 2006). This could be due to the lateral PFC's failure to hold task-relevant information when the task-irrelevant information interfered with working memory. Task-irrelevant information might cause more interference when if was in the same category as task-relevant information than when it was in a different category. Consistent with Yoon et al's study, Sakai and colleague found that greater dorso-lateral prefrontal cortex (DLPFC) activations were associated with successfully maintaining visual information even when performing a distractor task (Sakai, Rowe & Passingham, 2002). These results suggest the DLPFC is involved in actively maintaining information in working memory. In contrast, there are other studies suggesting that activation in the PFC is modulated by the demand of controlling task-irrelevant information (Jha et al., 2004). In Jha et al's study, participants were required to remember faces or visual objects. During the delay period, task-irrelevant items (either faces or visual objects) were presented. The participants had to indicate whether the probe matched one of the pictures they had remembered. Higher ventrolateral prefrontal cortex (VLPFC) activation was observed when the task-irrelevant information was in the same category as the items to be remembered and when the memory items were successfully remembered. In Sakai et al or Yoon et al's study, higher DLPFC activation was associated with better representation of memory stimuli whereas in Jha et al's study, higher VLPFC activation was associated with higher demand for resisting interference. This might reflect the functional heterogeneity of lateral PFC.

In summary, maintaining information in working memory may reduce visual processing of task-irrelevant information, and processing of task-irrelevant information during the memory delay interferes with memory maintenance. Interference was greater when the task-relevant information and task-irrelevant information were from the same category than from different categories. While these previous findings have provided insight into the effect of irrelevant visual process sing on working memory, the effect of encoding a new item on existing working memory and the effect of maintaining an item in working memory on encoding a new item have not be investigated. In multiple-item working memory tasks, all items were task-relevant. If two items are processed through different neural pathways, the interference between them is expected to be less than when they are processed in the same pathway. Thus, we expect to observe better recognition of items from different categories than items from the same category. In the next part, we will discuss whether there are different pathways for maintenance and processing of information from different categories.

1.4 Are there separate neural pathways for keeping information in working memory?

It has been shown that there are separate neural pathways for visual spatial and non-spatial information in the non-human primate brain (Ungerleider & Mishkin, 1982; Goldman-Rakic, 1987). Applying repetitive transcranial magnetic stimulation (rTMS) to the human DLPFC seems to impair visual spatial working memory while applying it to the VLPFC impairs visual object working memory (Mottaghy et al., 2002). Patients with superior frontal lesions demonstrate more working memory deficit in spatial tasks than non-spatial tasks (du Boisgueheneuc et al., 2006). However, inconsistent results have also been shown in monkeys (Rushworth et al., 1997) and humans (Owen et al., 1998).

ERP studies have also found different patterns between the visual spatial and non-spatial working memory tasks (Martín-Loeches & Rubia, 1997; Bosch, Mecklinger & Friederici et al., 2001). Previous ERP studies have found that a negative slow wave (NSW) is associated with visual working memory retention and it varies in amplitude with memory load (Bosch et al., 2001; Klaver et al., 1999; Klaver, Smid & Heinze, 1999; Mecklinger, & Pfeifer, 1996; Ruchkin et al., 1997). The scalp distribution of negative slow wave was different for the spatial and objects tasks. For example, Mecklinger and colleagues found that the amplitudes of the NSW at the frontal central and left temporal electrodes were sensitive to object working memory load while amplitudes at occipital and parietal electrodes were sensitive to the spatial working memory load (Mecklinger et al., 1996).

FMRI studies have shown that structures in the dorsal pathway, including the DLPFC, pre-supplementary motor cortex (preSMA), frontal eye field (FEF), superior parietal lobe (SPL) and intraparietal sulcus (IPS), are involved in spatial working memory tasks (Courtney, Petit, Maisog, Ungerleider, Haxby, 1998; Leung, Gore, Goldman-Rakic, 2002; Postle & D'Esposito, 1999; Smith, Jonides & Koeppe, 1996). In contrast, structures in the ventral pathway including the inferior temporal cortex and inferior frontal cortex are involved in visual object working memory tasks (Ranganath, Cohen, Dam & D'Esposito, 2004; Ranganath, DeGutis & D'Esposito, 2004). Some fMRI studies have directly compared visual spatial and non-spatial working memory tasks, and found differential activation patterns across these two conditions (McCarthy et al., 1996; Munk et al., 2002; Smith et al., 1995). However, other studies have not found consistent evidence supporting the dissociation of visual spatial and visual non-spatial working memory in the PFC (Owen et al., 1998; Postle et al., 1999; Postle, Stern, Rosen & Corkin, 2000; Sala, Rämä, & Courtney, 2003) but in posterior regions (Postle et al., 1999; Postle et al., 2000).

The inconsistent findings from human brain imaging studies could be due to the nature of the task requirements. Specifically, in the aforementioned studies, the spatial information and non-spatial information were presented at the same time while subjects were instructed to focus on remembering one aspect of them. The spatial and non-spatial information aspects of task items may be integrated or automatically coded and hence it may not be possible to extract and remember just a single aspect of the information.

In the lateral PFC, neurons showing preferences for objects are intermixed with those showing preferences for spatial locations and some neurons show a preference for both types of visual information (Rainer, Asaad & Miller, 1998; Rao, Rainer & Miller, 1997).

It has been shown that the visual association regions show functional specialization. The FFA and parahippocampal area (PPA) are found to be involved in face perception and scene perception respectively (Epstein & Kanwisher, 1998; Kanwisher, McDermott & Chun, 1997). Increasing the working memory requirement for faces and scenes increased activation in the FFA region and the PPA respectively (Druzgal & D'Esposito, 2001; Gazzaley et al., 2005; Ranganath et al., 2004).

In an extension to previous spatial and non-spatial studies, color and orientation were compared in some recent studies and independent activations were observed. Mohr and his colleagues examined working memory maintenance and manipulation of different feature including color and line orientation. In Mohr et al's study, the inferior frontal sulcus (IFS) was associated with maintaining and manipulating color and the junction of the SFS and pre-central sulcus (PrCS) was associated with maintaining and manipulating orientation (Mohr, Goebel & Linden, 2006).

It has been shown that a color perception task activated occipital and temporal regions including fusiform gyrus and lingual gyrus (Clark et al., 1997; Lueck et al., 1989; Sakai et al., 1995; Zeki et al 1991). A color discrimination task activated many more regions besides the lingual gyrus and fusiform gyrus, including the bilateral intraparietal sulcus (IPS), dorsal premotor (PM), SFS, inferior frontal gyrus (IFG) and preSMA (Claeys et al., 2004). In a more recent color working memory task, the left IFG was recruited in remembering colors. When controlling the verbalization on colors, right IFG was recruited (Ikeda & Osaka, 2007). They suggested that when remembering colors, the left IFG was associated with verbal information processing while the right IFG was associated with visual information processing. A frontal-parietal network, including the SFS, DLPFC, inferior parietal lobe (IPL) and SPL is involved in orientation maintenance (Cornette, Dupont, Bormans, Mortelmans, Orban , 2001; Cornette, Dupont, Salmon, Orban, 2001; Cornette, Dupont & Orban, 2002). Applying rTMS on the right PPC disrupted memory involving orientation (Prime, Vesia, & Crawford, 2008).

In the current study, we chose color and orientation as two separate categories. Instead of using the same item carrying information from both categories, the color and orientation were presented as separate items. Therefore, the dissociation between different features would not be confounded by feature integration.

1.5 How multiple items are represented in working memory

1.5.1 Neural computation models

Based on previous findings, there are at least two computational models of how multiple items are represented in working memory.

In one computational model, different stimuli are represented by different groups of neurons and different neurons serve different purposes. "Multiple working memory cells" show enhanced response to preferred stimuli and sustained activity when remembering multiple items. "Inferior temporal neurons" show activity to the preferred item and activity is disrupted by the subsequent item. "Prefrontal neurons" show sustained activity to the preferred stimulus only when the stimulus is the first in a sequence of stimuli (Amit et al., 2003; Yakovlev et al., 2005). Instead of proposing that there are specific neurons responding to items in multiple items working memory, another model has proposed that as the number of items in working memory increase, the synaptic signals as well as the connection among synapses increase (Macoveanu, Klingberg, & Tegner, 2006).

1.5.2 Animal studies

Single neuron recording studies with monkeys have demonstrated that when the monkeys had to view multiple objects, the inferior temporal cortex (IT) neurons showed the average activity as when they viewing the objects alone (Zoccolan, Cox, & Dicarlo, 2005). When remembering complex visual patterns, activities in the IT neurons were disrupted by inserting non-target items during the delay period whereas the PFC neurons continued firing although there was distractor (Miller, Erickson & Desimone, 1996). The neurons in PFC in monkeys have been found to be sensitive to specific items both in both spatial (Funahashi, Bruce & Goldman-Rakic, 1989) and non-spatial domains (Miller et al., 1996). When the items were presented in sequence, the monkey may not only encode object information, but the sequence order information. The neurons in the PFC have been found to exhibit activity pattern in response to an object as well as its order in the sequence and different neurons were sensitive to different items in a particular position in a sequence (Berdyyeva & Olson, 2009; Ninokura, Mushiake & Tanji, 2003, 2004). When remembering multiple items, the neurons in the PFC that respond to the first item were altered by adding a second item to working memory. Most neurons respond to both items (Warden & Miller, 2007). This study suggested that adding a second item in working memory seems to interfere with the representation of the first item.

Taken together, the single neuron recording studies in monkeys demonstrate that neurons that respond to visual stimuli are tuned by more than one item that they view. Presenting a new item disrupts the neuronal activity in the IT whereas adding a new item to working memory affects the neuronal activity of other items represented in the PFC.

1.5.3 Neuroimaging studies

Behavioral studies have suggested that the capacity of visual working memory in humans is limited to a few items. Luck and Vogel have found that visual working memory capacity is about four and is not affected by the property of the individual items (Luck & Vogel, 1997; Vogel et al., 2001). Brain imaging studies have showed that the activities in prefrontal cortex (PFC) and posterior parietal cortex (PPC) increase as memory load increases (Cohen et al., 1997; Smith & Jonides, 1997; Leung, Seelig, & Gore, 2004; Todd & Marois, 2004; Xu & Chun, 2006) but activity is attenuated at a load beyond capacity (Callicott et al., 1999; Leung et al., 2004). Event-related potential (ERP) studies have shown that the amplitude of a negative slow wave increases as working memory load increases (Löw et al., 1999; Mecklinger & Pfeifer, 1996; Vogel & Machizawa, 2004). Others have shown that the amplitude of P3 at the posterior electrodes decreases with increasing visual working memory load (Busch & Herrmann, 2003; Klaver, Smid & Heinze, 1999; McEvoy, Smith & Gevin, 1998; Morgan, Klein, Boehm, Shapiro, & Linden, 2008; Watter, Geffen & Geffen, 2001). Thus, the PFC or PPC might be the brain regions that maintaining visual information in working memory.

Recent visual working memory studies have focus on PPC besides PFC (See Xu & Chun, 2009 for a review). In particular, posterior parietal cortex, especially the IPS was found to be correlated with number of color discs maintained (Todd & Marois, 2004). Xu and Chun used simple and complex visual object and investigated the activation of IPS with working memory load. They found the inferior IPS was found to be correlated with number of items held in working memory while the superior IPS correlated with total number of features remembered (Xu & Chun, 2006). Song and Jiang (2006) found that the activity in SPL was affected by number of items as well as the feature. While the preSMA and IFS was responding to number of items, the lateral occipital lobe showed greater activity to complex feature (shape) than simple feature (color) (Song & Jiang, 2006). However, it is not clear whether multiple items from the same category and different category recruit the same set of brain regions. As shown in previous studies, distractor from different categories caused larger interference to working memory maintenance (Della Sala et al, 1999; Logie et al, 1990; Vuontela et al, 1999). When adding an item of the same category into working memory, greater impact on behavioral performance and greater activations in PFC and PPC are expected to be observed than adding an item of different category.

2. Specific aims of current studies

The current studies investigated how individual items in working memory interfere with each other and the neural correlates of representing multiple items in working memory. It has been shown that only a limited number of items can be held in working memory (Cowan, 2001; Luck & Vogel, 1997; Vogel, Woodman, & Luck, 2001). As the number of remembered items increases, the activity of the PFC increases (Cohen et al., 1997; Leung, Seelig, & Gore, 2004; Linden et al., 2003; Smith & Jonides, 1997). Between-item interference has been proposed to be the main source of forgetting (Oberauer & Kliegl, 2006). There are other types of interference that may cause forgetting, such as proactive interference (Underwood, 1957). According to Baddeley's (1986) model, information is being maintained and processed by modality-specific mechanisms. Evidence from neuroscience research has shown that there are distinct neural pathways for processing visual spatial and non-spatial information (Ungerleider & Mishkin, 1982: Goldman-Rakic, 1987). Interference or distraction from the cross-category stimuli caused less interference with working memory, while within-category distraction caused more interference (Logie, et al., 1990; Della Sala et al., 1999; Vuontela et al., 1999; Mohr & Linden, 2005). Previous studies examined the capacity of working memory in terms of how many items can be remembered and how the physical nature of an item may affect memory performance (Alvarez & Cavanagh, 2004; Eng et al., 2005; Luck & Vogel, 1997; Vogel et al., 2001). However, few studies have directly investigated interference between items in visual working memory or compared how the brain represents multiple items between cross-category condition and within-category condition.

In this dissertation, I examined between item competition or interference by examining the effect of adding a new item on an existing item in working memory and the effect of an existing item on the encoding and maintenance of a new item. We applied both behavioral and fMRI methods. In experiment 1A, we used color and orientation as stimuli in a two-item working memory task. The two items were either from the same category or from different categories. The purpose was to examine whether items of the different categories were remembered better than of same category. In experiment 1B, the participants had to remember one item and ignore the other. This experiment was to examine whether the performance differences between task conditions in experiment 1A was due to perceptual distraction. In experiment 2 and experiment 3, we manipulated the category of either the first or the second item and varied the category of the other item. We extended the findings for experiment 1 to more categories (color, orientation and shape). We examined whether holding an item in working memory had a larger effect on encoding a new item from the same category than from a different category. We also examined whether adding a new item into working memory interfered more with the existing item in working memory from the same category than from a different category. In experiment 4, we did a study with a longer delay outside the scanner and inside a 3T

MRI scanner. We examined whether activity in the lateral PFC increased when remembering items from the same category than remembering items from different categories.

3. Behavioral Experiments on Characterizing Interference between Items

It has been shown in previous studies that the memory for information from different feature dimensions or categories (such as color and orientation) is better than memory for from the same dimension or category (Kumar & Jiang, 2005; Olson & Jiang, 2002; Wheeler, & Treisman, 2002). These studies provided behavioral evidence for separate neural circuits for color and orientations. We conducted a set of three behavioral experiments to examine how maintaining an item in working memory affects encoding and remembering a new item and how encoding and remembering a new item influence an existing item in visual working memory. To determine the nature of interference, we used a delayed-recognition task in which the participants remembered two items and were tested on one of them. Behavioral data (Response Time and Accuracy) were recorded. Items from different feature categories were used (i.e., color, orientation, shape). In the first experiment, the participants had to remember two items with various combinations of color and line orientation. In the second experiment, we manipulated the category of the second item while keeping the category of the first item constant. In the third experiment, we manipulated the category of the first item while keeping the category of the second item constant. We hypothesize that adding an item to working memory would interfere with the existing memory and the existing memory would interfere with encoding and maintenance of a new item. The interference effect would be larger when items were from the same category than items from different category. Increased interference would cause lower accuracy and longer response time and be the main reason for forgetting in working memory.

3.1. Exp 1A (Comparison between the Within-category and the Cross-category Condition)

The purpose of this study was to examine the between-item interference in visual working memory. In this experiment, we used color and line orientation as stimuli's dimensions. Participants were required to remember two items. The two items were either from the same category (within-category condition: color-color or line-line) or different categories (between-category condition: color-line or line-color). At the probe stage, the participants had to make a decision on whether the item matched one of the items they remembered. We also used one-item working memory task as control (color or line condition). If color and line orientation were processed in completely different neural circuits and there was no interference between them, the performance should not differ between the one item and the item in the cross-category condition whereas the recognition rate should be greater in the cross-category condition than in the within-category condition. In contrast, if color and line orientation interfered with each other in working memory, the recognition rate of the cross-category condition should be greater than performance of within-category condition but worse that performance of remembering only one item.

3.1.1 Method

Participants

Twelve participants were recruited (range: 18 – 24 years old; mean age = 19.8; 5 males). Before the experiment, all participants were checked with vision acuity and color blindness (Ishihara, 1967). They had normal or correct to normal vision. Participants who failed to read the capital letters 10 feet away on a board were excluded (The visual angle of each letter is around 1 arc minute vertically from a 10 feet viewing distance). None of them had major neurological or psychiatric disorders based on a self-report interview. All participants were psychology undergraduates from Stony Brook University and they were compensated for research credit. Written consent was obtained from every participant and the research protocol was approved by the Institution Review Boards of Stony Brook University.

Procedure and analysis

Sixteen colors and sixteen line orientations were used as task stimuli (see Figure 1 and 2). The color stimuli were circles filled with different color. The line orientations were bars of different orientations. The participants were viewing the screen from about 3 feet away and the visual angle was around 3 degrees. The task paradigm was shown in Figure 4. At the beginning of a trial, a fixation (small cross) was presented for 500ms, followed by two stimuli presented consecutively in the center of the screen. The visual angle of the stimuli was around 3 degrees. The presentation time for each stimulus was 100ms. Short presentation time was used in order to reduce verbalization (Luck et al., 1997, Vogel et al., 2001). The interstimulus interval (ISI) between two items was 1500ms. After the disappearance of the second item and a 1500ms delay, a probe was presented in the center until a response was made. The cue number was presented above the probe. The participants were instructed to remember both stimuli and then made a judgment on whether the probe was same as the one indicated by the cue number in the memory list. If the cue number was 1, the participant was required to compare the probe with the first item. If the cue was 2, the participant was required to compare the probe with the second item. There were two types of probes: positive probe (which matches the item indicated by the number) and negative probe (which does not match any of the two items they remembered). Color negative probe was three items apart from the to-be-compared stimulus (i.e. if the to-be-compared stimuli was C4, the negative probe was either C1 or C7). Orientation negative probe was 33.75 degree apart from the to-be-compared stimuli. If the participant made a mistake, an "error" message would be shown on the screen. If no response was detected within 3 seconds, a "no response" message would be shown and the experiment proceeded to the next trial. The intertrial interval is 1000ms (See Figure 4A and 4B for paradigm).

Each participant completed a practice of 60 trials and a main experiment, which included 8 runs with a total of 256 trials. There are two types of task conditions: cross-category condition (color-color and line-line) and within-category condition (color-line and line-color). Each condition has equal number of trials. After the main experiment, there was a one-item control experiment task (Figure 4C), in which the participant only needs to remember one item (either color or line orientation) and made a response to the probe. There were 64 trials in the control task. Half of them were color items and half of them were line orientation items. The whole experiment took about 30 minutes to complete.

For the analysis on the main task, we did a 3-way analysis of variance (ANOVA) on item position (first/second item), feature (color/orientation) and condition (within-category/cross-category). To comparing the two-item task and the one-item control task, we did a two-way ANOVA on task condition (5 levels: first item in the within-category condition, first item in the within-category condition, second item in the cross-category condition, second item in the cross-category condition and one-item working memory task) and feature (color and orientation). The first four levels in the task factor were from the two-item working memory task while the fifth level in the task factor was from the one-item working memory task. Both accuracy and response time (RT) are analyzed by ANOVA.

The probability of positive and negative probe, testing of first and the second item, and testing of color and orientation were equal. The sequences were counterbalanced within and across subjects.

3.2.2 Results and Discussion

Accuracy

The results of accuracy are shown in Figure 5A and 5B. We found a significant main effect of position [$F(1, 11) = 20.223$, $p < .001$] and condition [$F(1, 11) = 9.576$, $p < .01$] and an approaching significant effect of feature [$F(1, 11) = 4.798$, $p = .051$] . The accuracy for the first item was lower than the accuracy for the second item. Accuracy in a the within-category condition was lower than that in a cross-category condition. The accuracy for orientation was lower than the accuracy for color. None of the interactions was significant. In the control task, the accuracy of color and orientation did not differ from each other [$t(11) < 1$].

In order to compare the one-item control task and the two-item task, we did a two-way ANOVA on task and feature. The main effect of task was significant ($F (4, 44) = 11.118$, $p < .001$). Further analysis suggested that accuracy for the item in the 1-item task was higher than accuracy of the first item (both the cross-category and the within-category conditions) in two item task ($ps < .05$) but not significantly different from second item in the 2-item task ($ps > .1$).

Response time (RT)

The results for response time are shown in Figure 5C and 5D. We found a significant main effect of feature [$F(1, 11) = 29.115$, $p < .001$]. The response to color was faster than the response time to orientation. The main effects of position and condition were not significant [position: $F(1, 11) = 2.183$, $p > .1$; feature: $F(1, 11) = 1.038$, $p > .1$]. The interaction of position*condition was significant [$F (1, 11) = 6.009$, $p < .05$]. This was because the response time for the second item in the within-category condition was slightly longer than in the cross-category condition. None of the other interactions was significant. The response time of the one color and one line in the one-item task did not significantly differ from each other [$t(11) = 1.78$, $p > .1$].

In order to compare one-item control task and two-item task, we did a two-way ANOVA on task and feature. The main effect of task was significant ($F (4, 44) = 31.552$, $p < .001$). The RT in the one-item task was faster than all conditions in the two-item task ($ps < .05$).

When load was increased from one item to two items, we observed lower accuracy and longer response time. Particularly, significant lower accuracy was only observed for the first item in two-item task when compared with one-item task. This suggests the representation was poorer when more than one items were held in working memory than when holding one item. This could be due to interference between items in working memory. An alternative reason could be attention. The participant paid more attention to the most recent item so that the accuracy for the second item was not significantly different from the accuracy in the one-item working memory task. However, this might not be the case. When remembering a sequence of items (> 3), the accuracy of the first item was higher than the intermediate items. If the participant paid more attention to the more recent item, they would observe lower accuracy for the first item than the intermediate items (Golob & Starr, 2004; McElree & Dosher, 1989). On the contrary, in sequential presentation, the first item would have chance of receiving more attention and rehearsal than the subsequent items so that its accuracy is higher than the intermediate items while the interference received by the last item was less than the intermediate items because there was no distractor presented afterwards (Atkinson and Shiffrin, 1968). So attention was less likely the reason that caused higher accuracy on the most recent item.

Consistent with previous findings, we observed higher accuracy for the cross-category condition than the within-category condition (Kumar & Jiang, 2005; Olson & Jiang, 2002; Wheeler, & Treisman, 2002). Although there was not overall response time difference between the within-category condition and the cross-category condition, the response time of the second item in the within-category condition was longer than the second item in the cross-category condition. These findings indicate that the accuracy was higher when the items were from different categories than from the same category, suggesting that color and orientation were represented by separate but interactive neural circuits. It has been shown in brain imaging studies that color and orientation are processed in different pathways (Mohr et al., 2006). However the present experiment suggested there was interference between color and orientation in working memory. Another source of interference could be the perceptual/attentional interference from each other and the perceptual interference could be greater in the within-category condition than in the within-category condition. To examine whether perceptual interference was the main source of interference, we conducted a control experiment in which the participants have to remember only one item and ignore the other item. If memory difference between two conditions are caused by perceptual interference, we would observe similar performance pattern in the following experiment.

3.2 Exp 1B: (Comparison between the Within-category and the Cross-category Condition: Perceptual Interference Control)

The purpose of this study was to find out whether lower accuracy in the within-category condition than in the cross-category condition was due to memory interference or perceptual interference. If the perceptual interference was the main reason for worse performance in the within-category condition, we would observe worse performance for remembering an item with a perceptual distractor than remembering one item in one-item task. We would also observe worse performance for the within-category condition than the cross-category condition.

Participants and Methods

Twelve adults participated in this study (range: 18 – 24 years old; mean age = 20.2; 2 males). Before the experiment, all participants were checked with vision acuity and color blindness (same way as in Exp 1A). They had normal or correct to normal vision. None of them had major neurological or psychiatric disorders based on a self-report interview. All participants were psychology undergraduates from Stony Brook University and they were compensated for research credit. Written consent was obtained from every participant and the research protocol was approved by the Institution Review Boards of Stony Brook University.

The design of this experiment was similar as Exp 1A except the subject only needed to remember one item (See Figure 4 for the paradigm). In both within-category and cross-category conditions, the participants were required to remember either the first or the second item. In four runs, they had to remember the first item while ignoring the second item and in another four runs, they had to remember the second item while ignoring the first item. Each run had 32 trials with equal number of trials in the the cross-category condition and the within-category condition, and equal number of trials with color probe and orientation probe. The two types of runs were counter balanced across subjects. A 3-way ANOVA on to-be-remembered item (first, second), feature (color, orientation) and condition (within-category, cross-category) was carried on the accuracy and response time. Same as exp1A, participants performed a one-item working memory task as control in the end of the main experiment. There were 64 trials in this one-item working memory task with half of the trials testing color and the other half testing orientation. To comparing one-item working memory control task with the main task, we did a two-way ANOVA on task (first item in the within-category condition, first item in the cross-category condition, second item in the within-category condition, second item in the cross-category condition and one-item condition) and feature (color and orientation).

Results and Discussion

The results are shown in Figure 6. Three-way ANOVA on accuracy have shown a main effect of condition ($F (1, 11) = 5.953$, $p < .05$). The accuracy for the cross-category condition was higher than accuracy for the within-category condition. Further pair-wise comparison between the cross-category and the within-category conditions revealed higher accuracy for remembering a color item following viewing an orientation item than following a color item ($t (11) = 2.461$, $p < .05$) and marginally higher accuracy of remembering an orientation item following viewing a color item than following an orientation item ($t (11) = 2.017$, $p = .069$). No other main effects or interactions were significant ($ps < .1$). The accuracy difference was not significant between one color and one line condition in the control task ($t (11) = 1.048$, $p > .1$). To compare one-item control task and the 2-item task, we did a two-way ANOVA on task and feature. The main effect of task was not significant ($F (4, 44) = 1.746$, $p > .1$).

Three way ANOVA on response time showed that main effect of feature was significant ($F (1, 11) = 9. 689$, $p < .05$). The response time of color was faster than the response time of orientation. The main effect of condition was approaching significance ($F (1, 11) = 4.539$, $p = .057$). Items in the cross-category condition were numerically faster than items in the cross-category condition (577ms vs 586ms). No other main effect of interaction was significant. The response time difference was not significant between one color and one line condition in the control task ($t (11) = 1.605$, $p > .1$). To compare one-item control task and the 2-item task, the two-way ANOVA suggested a main effect of task ($F(4, 44) = 6.839$, $p < .001$). Further analysis has shown that the RT of one-item was longer than the response time second items to be remembered ($ps < .05$).

Different from Exp 1A, we did not find significant accuracy differences between one-item control condition and any conditions in the two-item task. On the contrary, the response time in one-item control condition was longer than the second item in the two-item task. This suggests that one visual item without any distractor was not remembered better than that item presented with a distractor. When directly comparing the cross-category and the within-category conditions, we found a significant difference in accuracy for the second item but not for accuracy of remembering the first item. Response time of the within-category condition was slightly longer than response time of the cross-category condition (9ms longer). These effects could be due to some perceptual interference from the first stimulus. Concerning the accuracy for both the cross-category condition and the within-category condition was high (> .94), the perceptual interference could not have been the main source of interference between items in working memory observed in Exp 1A.

In previous studies (Yoon et al., 2007; Sreenivasan & Jha, 2005), researchers have found reduced accuracy when the distractor was congruent (the same category) with the memory item. They presented complex visual objects or adding a secondary task during the delay period. Different from theirs, the current study used simple features, and the distractor was just one item. The interference from one item might not be as strong as when presenting multiple items as distractor or inserting a secondary task.

To further examine interference between items, we included shape as another feature in the next two experiments.

3.3 Exp 2: Effect of Existing Working Memory on Encoding and Maintaining a New Item

This experiment examined how holding one item in working memory affected the encoding of a new item. The category of the first item was kept constant in color while we manipulated the feature categories of the second item. According to the results from Exp. 1A and previous research, we hypothesized that between-item interference would be stronger if the second item was of the same category as the item already held in working memory. We expected to find poorer performance on the second item when it was in the same category as the first item than when it was in a different category.

3.3.1 Method

Participants

Fourteen Stony Brook students were recruited (range: 18-23 years old; mean age = 20; 9 males). Before the experiment, all participants were checked with vision acuity and color blindness (same way as in Exp 1A). They had normal or correct to normal vision. None of them had major neurological or psychiatric disorders based on a self-report interview. All participants were psychology undergraduates from Stony Brook University and they were compensated for research credit. Written consent was obtained from every participant and the research protocol was approved by the Institution Review Boards of Stony Brook University.

Method and Analysis

The task paradigm was shown in Figure 7. Sixteen colors circles, sixteen lines of different orientations and sixteen shapes were used as stimuli (See Figure 1, 2, 3 for stimuli).

The design of the two-item working memory task was similar as that in Exp 1A except the task conditions. There were three conditions (color-color, color-line and color-shape). Besides, there was a one-item working memory task as control, in which the participant only needed to remember one item (either color, orientation or shape) and made a response to the probe. Each participant completed a practice of 40 trials and the main experiment, which included 6 parts with a total of 192 trials. Each condition had 64 trials. There were 96 trials in the control task with 32 trials in each condition. The whole experiment took about 40 minutes to complete. The probability of positive and negative probe, testing of first and the second item, and testing of color and orientation were equal the sequences of conditions were counterbalanced within subjects.

For the analysis, we did a 2-way ANOVA on position (first, second) and condition (color-color, color-line and color-shape). To comparing items in the control task and item in the main task, we did another 2-way ANOVA on task (the second item in the main task and one-item task) and feature (color, orientation and shape).

3.3.2 Results and Discussion

Accuracy

The accuracy data are shown in Figure 8A and 8B. The main effect of position was significant ($F(1, 13) = 15.557$, $p < .01$). The accuracy for the first item was lower than the second item. The main effect of condition was approaching significance ($F(2, 26) = 3.222$, $p = .056$). Further analysis showed that the accuracy of color-shape condition was lower than that of color-line condition ($p < .05$, Bonferroni corrected). The interaction of position and condition was approaching significance ($F(2, 26) = 3.078$, $p = .063$). It was due to the lower accuracy of the first color followed by shape than the color followed by line. In the 2-way ANOVA comparing the control task and the main task, we found a main effect of task ($F(1, 13) = 8.876$, $p < .05$). The accuracy of one-item task was higher than the accuracy of the second item in the two-item working memory task. Average accuracy for the three features did show significant differences either in the main task nor in the control task ($ps > .1$).

Response time

Response time data are shown in Figure 8C and 8D. The main effects of position and condition were not significant ($ps > .1$). The interaction was significant ($F(2, 26) = 10.229$, $p < .001$). Further analysis showed that response time was longer for the first item than the second item in color-color condition while it is opposite in color-shape condition (color-color: $t(13) = 2.247$, $p < .05$; color-shape: $t(13) = 3.298$, $p < .01$). The main effect of feature in the control task was not significant ($F(1, 13) < 1$). In the 2-way ANOVA comparing control task and main task, we found a main effect of task ($F(1, 13) = 85.159$, $p < .001$). The RT in the one-item task was faster than the RT in the second item in the main task. The effect of three features was not significant in the two-item working memory task or in the control task ($ps > .1$).

Consistent with experiment 1A, the accuracy was lower for the first item than for the second item. When remembering a second item when having maintained one item in working memory, RT was slower and accuracy was lower as compared with remembering one item. However, there were no significant interference differences among different categories. We observed some trend to longer RT and lower accuracy for the color after the color item than the color after line or shape. These findings suggest that interference in existing memory on encoding a new item is weak so we are not able to differentiate within-item or cross-item conditions. In experiment 3, we manipulated the category of the first item and have the category of the second item constant. We expected to find larger interference for adding a new item on existing memory when they were from the same category than when they were from different category.

3.4 Exp 3: Effect of Encoding and Maintaining a New Item on Existing Working Memory

This experiment was to examine how encoding and maintaining a new item interfered on existing working memory. The category of the second item was kept constant in color while we manipulated the feature categories of the first item. We expected to observe larger interference when the two items were from the same category than from different categories.

Participants

Twelve Stony Brook students were recruited (18 – 24 years old, mean age = 20.5 years old, 7 males). Before the experiment, all participants were checked with vision acuity and color blindness (same way as in Exp 1A). They had normal or correct to normal vision. None of them had major neurological or psychiatric disorders based on a self-report interview. All participants were psychology undergraduates from Stony Brook University and they were compensated for research credit. Written consent was obtained from every participant and the research protocol was approved by the Institution Review Boards of Stony Brook University.

Method

This study was similar to experiment 2 except for the tasks. There were three conditions: color-color, line-color, and shape-color. The control task was the same as experiment 2 (Figure 9).

For the analysis, we did a 2-way ANOVA on position (first, second) and condition (color-color, line-color and shape-color). To comparing items in the control task and item in the main task, we did another 2-way ANOVA on task (the first item in the main task and one-item task) and feature (color, line and shape).

Results and Discussion

Results of accuracy are shown in Figure 10A and 10B. The main effect of position was significant ($F(1, 11) = 6.068$, $p < .05$) with the accuracy of the first item lower than the second item. The interaction of position and condition was significant as well ($F(2, 22) = 4.25$, $p < .05$). The accuracy differences among three conditions were significant for the first item ($F(2, 22) = 4.592$, $p < .05$) whereas they did not reach significance for the second item ($F < 1$). Particularly, accuracy of the first color was lower than the accuracy of first shape ($p < .01$, Bonferroni corrected). The main effect of condition was not significant ($F(2, 22) = 1.125$, $p > .1$). In the 2-way ANOVA comparing control task and the main task, we found a main effect of task ($F(1, 11) = 14.474$, $p < .01$). The accuracy of item in the one-item working memory task was higher than the first item in the two-item working memory task. The average accuracy of color, orientation and shape in the one-item working memory task were .969, .958 and .964 respectively and the differences did not reach significance ($F(1, 11) < 1$).

Results of RT are shown in Figure 10C and 10D. The main effects of position and condition were significant (position: $F(1, 11) = 9.159$, $p < .05$;condition: $F(1, 22) = 7.328$, $p < .01$). The response time for the second item was faster than the first item. The response time for the items in the color-color condition was faster than the items in the color-line condition. The interaction were not significant ($F(2, 22) = 2.489, p > .1$). In the 2-way ANOVA comparing control task and the main task, we found a main effect of task ($F(1, 11) = 22.237, p < .001$). The response time for item in the one-item working memory task was faster than the first item in the two-item working memory task. The RT of color, orientation and shape in the one-item working memory task were 552ms, 554ms and 548ms respectively and the differences were not significant ($F(2, 22) < 1$). However, the response time differences among three features of the first item in the two-item working memory task were significant ($F(2, 22) = 7.337, p < .01$). Particularly, response time of the first line was longer than the response time of the first color or shape ($ps < .05$, Bonferroni corrected).

Consistent with experiment 1A, accuracy of the first item decreased and response time increased when adding a new item to existing working memory. As suggested in experiment 1A, the longer response time and lower accuracy of the first item compared with one item condition was caused by between-item interference. However, the accuracy and response time data were somewhat contradictory with our expectation of between-item interference effect. The accuracy of the first color was lower than the first shape while the response of the first color was faster than line. If we only compared color and shape, we could still accept the hypothesis that interference was larger when adding a new item of the same category into working memory than adding a new item of different category. This was consistent when we use color and line as stimuli in experiment 1A. Taken together, when we use more than 2 features, the data were not too consistent. Future studies will be including only color and shape as stimuli and examining interference between these two features.

3.5 Summary of behavioral results

The behavioral experiment demonstrated that accuracy was higher and response time was shorter for recognizing simple visual feature (color and line orientation) in the cross-category condition than in the within-category condition. Compared to the single item task, recognition of any items in the two-item task was worse, no matter whether they were in the cross-category condition or the within-category condition. There were perceptual effects but the main source of performance difference in remembering two items appear to be caused by between-item competition or interference. The second item has a greater effect on the first item than the other way.

The item position effect in a serial presentation has been extensively studied. Consistent with previous findings, it has been shown that the most recent item was remembered the best (Broadbent, & Broadbent, 1981; Jiang, 2004; Jiang & Kumar, 2004; Kumar & Jiang, 2005). Between-item interference has been proposed to a major source for forgetting in working memory (Oberauer & Kliegl, 2001, 2006; Oberauer & Lewandowsky, 2008).

Findings from the current study suggested that adding a new item into working memory interfered with the current work memory and may result in poorer representation. While accuracy for the second item was higher than for the first item in experiment 1A, the accuracy or response time differences were not significant between the first and the second item in experiment 1B. In addition, accuracy was lower and response time was longer for the second item in two-item working memory task than in one-item working memory task of experiment 1A, whereas the trend was not observed for accuracy and response time in experiment 1B. These findings could be taken as evidence that it was the interference between items in working memory rather than perceptual interference that caused the worse performance for the first item.

The behavioral experiments have found that the features from different categories produced less interference than feature from the same category. It has been suggested that spatial and non-spatial information are processed in different pathways (Goldman-Rakic, 1987; Ungerleider & Mishkin, 1982). It has been further suggested that color and line orientation are represented by different neural circuits and cause little interfere on each other in a dual task (Mohr et al., 2006; Mohr & Linden, 2005). While the interference from the first item to the second item was too weak to differentiate between the cross-category and the within-category, the interference from the second item to the first item was stronger in the within-category condition than in the cross-category condition to some extent. However, data from experiment 3 were not clear and further examination would be needed.

Some previous findings have found that features from different categories (such as color and line orientation) are better remembered than features from the same category (Kumar & Jiang, 2005; Olson & Jiang, 2002; Wheeler & Treisman, 2002). Findings from the current studies are consistent with those studies. The advantage of the current design as compared to previous studies was that the items were presented individually, thus removed the potential effect from feature integration of spatial configuration. In most previous studies, features were either from part of an object or more than one item was displayed at the same time. It was possible that the participants were grouping features as a whole when features were presenting together (Wheeler & Treisman, 2002; Xu, 2002). Grouping may be another factor that affecting how items were remembered so that be confound with interference. When more than one item was presented, the spatial configuration may affect recognition (Jiang, Olson, & Chun, 2000).

However, the response time results were inconsistent across the current experiments. Response time was longer for one-item working memory control task than the second item in the main task in experiment 1B and it was faster for the first orientation than for first color in experiment 3. One possible reason could be the speed-accuracy trade-off: faster response time was associated with lower accuracy. Another possible reason could be that the response time was not sensitive to feature change in working memory. Since response time data were not reported in previous studies of the same nature (Kumar & Jiang, 2005; Makovski, Sussman, & Jiang, 2008; Olson & Jiang, 2002; Xu, 2002), it is not possible to compare the results.

In sum, adding an item to working memory had a greater impact on later recognition of the existing item and interference was stronger when items were from the same category than when items were from different category. To examine the neural correlates of representing multiple items in working memory, we did an fMRI study.

4 Neural correlates of multiple-item working memory

The second aim was to investigate the brain representation of multiple-item working memory. Human fMRI studies have shown that frontal and parietal activity increases as memory load increases (Cohen et al., 1997; Smith & Jonides, 1997; Leung, Seelig, & Gore, 2004; Todd, & Marois, 2004). However, it is unclear whether the prefrontal and parietal areas are equally involved in representing multiple items of the same category or different categories.

The paradigm was similar as in experiment 1A. The participants were either remembering one item (color or line) as control condition or remembering two items. The two items were either from the same category (line-line) or from different categories (color-line or line-color). We mainly examined the effect of adding a line item on the representation of an existing item in working memory. We used orientation as the key task stimuli because orientation elicited consistent and reliable activations in the lateral PFC, middle temporal cortex and posterior parietal cortex in our pilot fMRI study. We expected to observe larger lateral PFC especially the DLPFC activation for remembering two items from the same category than from different categories.

4.1 Exp 4A (Multiple Item Working Memory: an fMRI Experiment -- Outside the Scanner)

The purpose for this study was to test the feasibility of our fMRI design.

4.1.1 Participants

17 healthy subjects from Stony Brook University were recruited for this study (range: 18 – 24 years old, mean age = 20.4, 6 males). Before the experiment, all participants were checked with vision acuity and color blindness (same way as in Exp 1A). They had normal or corrected to normal vision. None of them had major neurological or psychiatric disorders based on a self-report interview. All participants were psychology undergraduates from Stony Brook University and they were compensated for research credit. Written consent was obtained from every participant and the research protocol was approved by the Institution Review Boards of Stony Brook University. Two were removed from final analysis because of accuracy were at chance level for one line condition. So 15 participants were included in final analysis.

4.1.2 Method

The task paradigm is shown in Figure 11A and 11B. The stimuli used were same as in Exp 1A. In the beginning of the trial, there was a fixation of 2 seconds. After that, there were either one or two stimuli presented. Each stimulus was presented for 100ms. The ISI was 500ms. It was shorter than in behavior experiment because we wanted to use the time efficiently in fMRI study. After the presentation of the stimuli, there was a delay of 8.3 seconds, followed by the probe. The probe stayed on the screen for 1 second. The participant had to make a response on whether the probe matched one of the item presented before the delay. They were asked to make quick responses. The ITI was 1.5 seconds.

There were five task conditions: one color, one line, line-line, line-color and color-line. We did not include color-color condition because we were mainly focusing one feature: how adding an orientation to working memory interfered with working memory. This reduced the number of trials for fMRI study. There were 24 trials in each condition and a total of 120 trials. The probability of positive and negative probes was equal. Participants finished a practice of 2 runs before the 8 run experiment. In each run, there were 3 trials of each condition and there were 15 trials totally in each run. The sequence of the runs was counter-balanced across participants. The whole experiment took 40 minutes to finish.

4.1.3 Results and Discussion

Accuracy

Accuracy data is shown in Figure 12A. For data analysis, we divided conditions based on the probe type. For the line probe, there were three conditions: one line, line-mix (line probe in either color-line or line-color conditions) and two lines. The accuracy for these three conditions were .916, .915 and .904 respectively and the one-way ANOVA showed that the main effect was not significant ($F< 1$). For color probe, the accuracy difference between one color and color-mix (color probe in color-line or line-color condition) was not significant after paired t-test ($t = 1.662$, $p > .1$).

Response time

Response time data is shown in Figure 12B. The main effects on response time in among the line probe conditions were significant ($F(2, 28) = 19.432$, $p < .001$). Response time in both line-line and line-mix condition were longer than in the one line condition ($ps < .01$). Line-line condition was marginal longer than in the line-mix condition ($p = .086$). For color probes, the response time to one color was longer than that to the color-mix ($t(14) = 4.739$, $p < .001$).

In sum, accuracy of items from the same category (line-line) was numerically lower than items from different category (line-mix) but the differences were not significant. As hypothesized, the response time was longer in line-line condition than in one line or line-mix conditions. It suggested it was harder to retrieve orientation information when the two items held are from the same category than from different categories.

4.2 Exp 4B (Multiple Item Working Memory: an fMRI Experiment -- Inside the Scanner)

This experiment with fMRI experiment used a similar paradigm as Exp 4A. We used an event-related design for this study. This aim of this experiment was to examine whether activation of lateral PFC especially DLPFC increased when remembering two items from the same category than from different categories.

4.2.1 Participants and Method

Sixteen healthy subjects participated in this study (range: 19 – 27 years old, mean age =4, 9 males). Before the experiment, all participants were checked with vision acuity and color blindness (same way as in Exp 1A). They had normal or correct to normal vision. None of them had major neurological or psychiatric disorders based on a self-report interview. Participants were recruited from Stony Brook area by posting fliers on Stony Brook campus. Regular smokers and drinkers were excluded from current study. Written consent was obtained from every participant and the research protocol was approved by the Institution Review Boards of Stony Brook University. They were compensate 30$ for their participation.

We used the same stimulus as Exp 1. The paradigm was same as Exp 4A but extended fixation time (3s) and ITI (variable: 9.5s, 11s and 14s). Each ITI level had an equal chance of appearance and equal chance of preceding each condition level. They were given a practice of 2 runs the day before the fMRI study.

4.2.2 Data acquisition and analysis

Data was collected on a 3T Philips Achieva system using the standard quadrature head coil (8 channels). Twenty-four axial-oblique slices (5mm thickness) were prescribed parallel to the anterior-posterior commisural (AC-PC) line. The acquisition parameters for the inplane anatomical images were as follows: repetition time (TR) = 300ms, echo time (TE) = 5ms, Flip angle = 60 degree, field of view (FOV) = 220x220 mm, matrix = 256x256. The acquisition parameters for the EPI images were as follows: TR = 1.5s, TE = 30ms, Flip angle = 80 degree, FOV = 220x220 mm, matrix = 64x64. This resulted in a voxel size of 3.4x3.4x5mm. We used ascending acquisition from the bottom slice. There were 245 image volumes collected in one scanning run. We used a parallel imaging acquisition with an acceleration factor of 2. The acquisition parameters for the high resolution anatomical images were as follows: TR = 2530ms, TE = 4.6ms, Flip angle = 8 degree, FOV = 250x200 mm, matrix = 64x64.

During the scanning, subjects were in supine position in the scanner and view through a mirror on top of the head coil. The display was projected on the screen placed at head of the scanner bore. On seeing the probe, the participants had to use their left index or middle finger to press the left or right bottom. The key designation for “Yes” and “No” responses was counterbalance across participants.

We used SPM2 for image preprocessing and analysis (http://www.fil.ion.ucl.ac.uk/spm/). Images were first reoriented and slice time corrected for difference slices. Then the motion correction were performed and runs with motion greater than 3mm in x, y or z dimensions or 1.5 degrees in pitch, yaw or roll angles were removed from analysis. The EPI images were co-registered with the inplane and high resolution anatomical images. Anatomical images were segmented (grey and white matter) and normalized to the MNI grey matter template using a 12-parameter affine registration followed by nonlinear transformations. Then the normalized images were smoothed using a Gaussian filter with full width at half maximum of 8mm. We also set a high pass level at 1/128 HZ to filter low frequency signals (such as linear drifts)

For individual data analysis, each dataset were analyzed by constructing a general linear model (GLM). We first defined three events (encoding, mid-delay and probe). The onset time for these events were 3s, 7.8s and 12s for two-item working memory tasks and 3.6s, 7.8s and 12s for one-item working memory tasks. The duration of these events were 0s, 0s and 2s. Each event was used as a regressor and convolved with hemodynamic responses. Motion parameters were set as covariates to remove motion related activities. For each individual, t-tests were performed for each voxel on the estimated parameters of the regressors (beta weights) between each events and baseline or between different events (e.g. one color v.s. one line at delay stage).

For group data analysis, we conducted random effects analysis between conditions of interests. One-sample t-test was carried on the condition of interests using the contrast values from individual subjects. These included the comparison between different conditions during the encoding stage and delay stage. All final group data analysis were corrected by false discovery rate (Genovese, Lazar & Nichols, 2002). For visualization, final t values were overlaid on average normalized high resolution brain maps.

We extracted regions of interest (ROIs) based on the activations in one-item control condition and their comparisons. They included conjunction activation of one color and one line, one color, one line, and the contrast of one color versus one line. These contrasts were combining encoding and mid-delay stages. ROIs were extracted as a sphere of 8mm centered at the peak coordinates of the cluster. The ROI sphere was equal of the size of 79 voxels. Error trials and motion trials were removed from analysis. With these ROIs, we calculated the percentage signal change at the delay stage of each individual task conditions and then used one-way ANOVA to analysis the values.

4.2.3 Results and Discussion

Behavior results

The Behavioral results are shown in Figure 13. The data were analyzed by the probe type. Based on the probe type and conditions, there were five task conditions: one color, color-mix (color probe in color-line or line-color conditions), one line, line-mix (line probe in color-line or line-color conditions) and line-line (line probe in line-line condition). The accuracy main effect of task in line probe conditions was significance ($F(2, 30) = 4.698$, $p < .05$). The accuracy of line-line condition were lower than line-mix ($p = .051$). It suggested that item was remembered better in cross-category condition than in within-category condition. Pairwise t-tests showed that the differences between one color and color-mix were not significant ($ts < 1$).

One-way ANOVA on the response time of line probe conditions showed a significant main effect ($F(2, 30) = 39.562$, $p < .001$). The response time of one-line condition was faster than the response time of line-mix and line-line condition ($ps < .001$, Bonferroni corrected). The response time difference between one color and color-mix conditions was not significant ($t(12) = 1.44$, $p > .1$).

Color and orientation related activations

We used the regions which showed supra-threshold activity during the encoding and delay epochs of one color or one line condition compared with baseline as ROIs. The regions that showed supra-threshold activity in the contrast of one color and one line condition were also included. The ROI data were extracted using a sphere of 8mm using the peak coordinates as the center. With these cluster, we then calculated the percentile change signal of the delay stage of each condition. See Table 1 for cluster location and Figure 14 for activation map.

We predicted four possible patterns. If a region was sensitive to color than orientation, it should show higher level of activity in one color, color-line and line-color condition than in one line or the line-line condition (Figure 15A). If a region was sensitive to orientation than color, it should show the highest level of activation in the line-line condition and the lowest level of activation in the one color condition (Figure 15B). If a region was sensitive to number of items, it should show higher level of activation in the line-line, color-line and line-color conditions than one color or one line conditions (Figure 15C). If a region was recruited when remembering two items from the same category than from different category, it should show the highest level of activation in the line-line condition and the lowest in one color or one line condition (Figure 15D). To analysis the role of these clusters, we did a one-way ANOVA on the percentage signal change obtained from the five conditions.

In the conjunction activations of one color and one line condition, activitions in bilateral fusiform, left IPS, PrCS, right insular, middle frontal gyrus (MFG), preSMA and SMA were observed. Bilateral lingual gyrus showed higher activity in one color condition than in one line condition. Bilateral dorsal PFC, SPL, IPS, pre-central gyrus (PrCG), left middle temporal gyrus (MTG), precuneus and right inferior temporal gyrus (ITG) showed higher activity in one line condition than in one color condition ($p < .05$, FDR corrected, cluster size > =9).

The two lingual gyrus clusters, although showed heightened activation in one color condition in encoding stage, did not showed significant differences from one line condition during mid-delay stage (Figure 16).

Brain activities associated with adding one line into working memory

The main focus of the current study was to examine what brain region is involved when adding a line item to existing working memory. We compared line-color or color-line with one color condition. The bilateral SPL (extended to IPS and IPL) and left dorsal PFC showed greater activation in line-color or color-line condition than in one color condition ($p < .05$, FDR corrected, cluster size > =9). When subtracting one line from the line-line condition, we found activations more widely spread in the frontal and parietal regions including the bilateral dorsal PFC, MFG, IPS (extended to IPL) and SPL and preSMA, ($p < .05$, FDR corrected, cluster size > =9) (Figure 17A, 17B, 17C).

A few ROI clusters in showed heightened activity in remembering orientation than remembering color. These clusters located in bilateral IPS, SPL and the left dorsal PFC and they were involved in maintaining orientation as the level of activation were highest in the line-line condition and lowest in one color condition. All of these clusters showed significant main effect of condition ($ps < .001$). The level of activation in one color condition was lowest among all conditions and the line-line condition was highest among all conditions ($ps < .05$, after Bonferroni correction), and the color-line, line-color and one line condition did not show significant difference between each other ($ps > .1$) (Figure 18).

Brain activities associated with representing number of items

Among the ROIs, the left ventral posterior IPS (MNI coordinates: -30 -66 39) was involved in representing number of items as it showed increased level of activations to increased number of items. It showed significant main effect of condition ($p < .001$). The level of activation of one color was lower than color-line, line-color or line-line condition (color vs color-line: $p = .057$; color vs line-color: $p < .05$; color vs line-line: $p < .05$). The level of activation of one line was lower than the color-line, line-color or line-line condition ($ps <.05$, after Bonferroni correction) (Figure 19A).

To find out whether other regions are involved in representing number of items, we did a conjunction analysis on all three two-item working memory conditions (color-line, line-color and line-line). A cluster in left PrCG (MNI coordinates: -30 6 30) showed greater activities in remembering two items than remembering one item. The main effect of condition was significant ($p < .001$). The level of activation of color was lower than color-line, line-color and line-line condition (color vs color-line: $p = .061$; color vs line-color: $p < .05$; color vs line-line: $p < .05$, after Bonferroni correction). The level of activation of one line was lower than the color-line, line-color or line-line condition (color vs color-line: $p < .05$; color vs line-color: $p < .072$; color vs line-line: $p < .05$, after Bonferroni correction) (Figure 19B).

Remembering two items from the same category vs remembering items from different category

Greater activations were observed in the bilateral dorsal PFC, IPS, SPL, MTG and right PrCS in the line-line condition compared to the color-line or line-color conditions ($p < .05$, FDR corrected, cluster size < =9) (Figure 20A, 20B). In the last session, I have mentioned the brain regions recruited when adding a line item into working memory: in the “line-color vs color” comparison, a color item was added to the orientation working memory and in the “line-line vs line” comparison, a line item was added to the orientation working memory. When subtracting these two comparisons, we did not find any significant clusters at $p < .05$, FDR corrected. However, when we lower the threshold ($p < .001$, uncorrected, cluster size > =9), the right dorsal PFC (extended to FEF) and IPS were observed (Figure 21). These two pieces of evidence suggested that the dorsal PFC and IPS are more active when remembering two orientations compared to remembering a mixture of color and orientation items.

Among the ROIs, the right PrCS (MNI coordinates: 54 9 24) showed greater level of activity in the within-category condition than in the cross-category conditions. The main effect of condition was significant ($p < .001$). The level of activation of the line-line condition was higher than that of all the other conditions (ps <.05, after Bonferroni correction) (Figure 22).

4.3 Summary of fMRI Results

When adding a line item into working memory, a network of prefrontal parietal regions including IPS, SPL, IPL, PrCS and dorsal PFC was recruited. Greater enhancement was observed in right dorsal PFC, IPS and PrCS in within-category condition than in cross-category condition. Greater activations in bilateral dorsal PFC, IPS, SPL, MTG and right PrCS were found in line-line condition than in color-line or line-color condition. In contrast, the left ventral posterior IPS and PrCG were more involved in representing number of items, disregarding whether they are both orientations or an orientation and a color.

The lingual gyrus and the medial visual cortex showed greater activation for color than for orientation condition while the dorsal PFC and posterior parietal cortex showed greater activation for orientation than for color condition. It was consistent with previous findings (Clark et al., 1997; Cornette, Dupont, Bormans et al., 2001; Cornette, Dupont, Salmon et al., 2001; Cornette et al., 2002; Lueck et al., 1989; Sakai et al., 1995; Zeki et al 1991). A network of prefrontal and parietal regions showed activities in both remembering one color and remembering one orientation. Within these neural circuits, we have located a few clusters which were associated with orientation memory. These include bilateral IPS, SPL and left dorsal PFC. The left ventral posterior IPS was representing number of items and the right PrCS showed greatest activity in within-category condition than all the other conditions.

When adding a line item to working memory, the IPS, SPL, IPL, PrCS and dorsal PFC were recruited. These regions were suggested to be involved in remembering spatial information (Courtney et al., 1998; Leung et al., 2004; Postle & D'Esposito, 1999; Smith et al., 1996) or orientations in working memory (Cornette, Dupont, Bormans et al., 2001; Cornette, Dupont, Salmon et al., 2001; Cornette et al., 2002; Mohr et al., 2006).

Greater activation were observed in posterior parietal regions including the IPS, SPL, as well in bilateral MTG and right PrCS when holding two items in the within-category condition than in the cross-category condition. As there were two items in both conditions, such activity could not be due to number of items. Instead, as there was one more line item in the line-line condition than the color-line or line-color, these activations could be due to orientation working memory. These regions in posterior parietal cortex overlapped with orientation working memory circuit shown in previous studies (Cornette, Dupont, Bormans et al., 2001; Cornette, Dupont, Salmon et al., 2001; Cornette et al., 2002; Mohr et al., 2006). An alternative reason was that these activities could be due to interference between items. As color and orientation were processed in different pathways to some extent and two items from the different categories were remembered between than two items from the same category, these facts could reflect larger interference between items in within-category condition than in cross-category condition. Moreover, the right dorsal PFC and IPS showed a larger increment when remembering two orientations than when remembering a color and an orientation. This increment could not be explained as orientation working memory as it was from adding a line to a line item than adding a color to a line item. This dorsal prefrontal region, along with the posterior parietal region which showed greater activation for remembering two orientations than remembering two items from different categories, were part of the visual spatial working memory circuit (Courtney et al., 1998; Leung, Gore, & Goldman-Rakic, 2002; Leung et al., 2004; Rowe & Passingham, 2001) and may be involved in representing multiple visual items (Todd & Marois, 2004; Xu & Chun, 2006). The dorsal PFC and posterior parietal network may be involved in holding task information and resisting interference between items.

In sum, adding a line orientation item into working memory recruited a neural network of prefrontal and posterior parietal cortex including IPS, SPL, IPL, PrCS and dorsal PFC. The activation enhancement was larger when remembering two items from the same category than from different categories. This network might be involved in representation task information and resisting interference between items.

5 General discussion

The current study investigated multiple item working memory using behavioral measures and fMRI methods. The behavior studies showed that the simple features in the one-item working memory task were maintained better than features in the two-item working memory task, and the features from the cross-category condition were maintained better than features from the within-category condition in the two-item working memory task. Memory deterioration was mainly caused by interference between items in working memory instead of perceptual interference. The second item has a stronger impact on remembering the first item than vice versa.

Differential activations were observed between color and orientation. Bilateral IPS, SPL and left dorsal PFC showed greater responses to orientation items than to color items whereas the left ventral posterior IPS and PrCG showed increases activations in response to number of items regardless of the specific feature of the items. The right dorsal PFC, IPS, SPL, MTG and right PrCS showed a larger increment in activation when remembering two orientations than when remembering a color and an orientation. The right PrCS showed greater responses to two orientations than to the other conditions.

5.1 Interference between items in visual working memory

Decay and interference are two main causes of forgetting during short-term memory (Brown & Brown, 1958; Peterson & Peterson, 1959). Recently Oberauer and his colleague's studies suggested that forgetting is mainly caused by the interference between items in working memory (Oberauer & Kliegl, 2001, 2006; Oberauer & Lewandowsky, 2008). In their interference model, they suggested that items sharing same feature would compete and lose information. The findings in our studies supported their model.

It has been suggested that color and orientation are processed in different pathways (Mohr et al., 2006). If different features are indeed processed in different neural circuits or different pathways and there is no interference between these pathways, adding an item of different category would cause no interference to the existing working memory. However, none of the current behavioral experiment supports this hypothesis. When number of to-be-remembered item increased from one to two, accuracy decreased and response time increased. This suggests there is interference between items no matter whether they were from the same category or different categories. However presenting a distractor along with the remembered item did not produce lower performance than remembering one item. The results from experiment 1A and 1B confirmed that the interference between items was interference in memory instead of perceptual interference. More information about interaction between pathways was discussed in the following section.

We hypothesized that the interference was larger in the within-category condition than in the cross-category condition. Results from our first experiment supported this hypothesis. In experiment 2 and 3, we did find some support to our hypothesis. The data showed that holding an item in working memory weakly interferes with the encoding of a new item of the same category than of different category. In addition, adding a new item into working memory produced a larger interference on the feature of the same category than of different category except response time data in experiment 3 contradicted this. As shape was an extra feature added to experiment 2 and 3 compared with experiment 1, we would need to examine interference between color and shape in a future study.

It has been shown in previous memory tasks that the accuracy of the memory for most recent item or display in sequence is the highest (Broadbent, & Broadbent, 1981; Jiang, 2004; Jiang & Kumar, 2004; Kumar & Jiang, 2005). Consistent with previous findings, when remembering two items, adding a new item had more impact on the working memory of the first item than vice versa. When remembering one item with a distractor (in experiment 1B), the second item was not remembered better than the first one. This again confirmed that the worse performance for the first item than the second item was not due to perceptual interference.

5.2 Feature based v.s. item based representation in working memory

In previous visual working memory studies, it has been shown that posterior parietal cortex was functionally segregated (Xu & Chun, 2006, Song & Jiang, 2006). Different regions responded to different features (Song & Jiang, 2006) and activations in IPS correlated with number of items held in working memory (Todd & Marois, 2004). In the current study, we found bilateral SPL and IPS responding to orientation working memory. This was consistent with previous finding that dorsal parietal is involved in orientation processing and maintenance (Cornette, Dupont, Bormans et al, 2001; Cornette, Dupont, Salmon et al, 2001; Cornette et al, 2002). On the contrary, although the lingual gyrus showed greater activity for the color than for the orientation, the activity was mainly observed at the encoding stage. Some frontal regions including the SMA, left MFG and right insular were found to be activated in conjunction analysis of color and orientation, and they did not show differences between different conditions. Other part of the posterior parietal cortex, left ventral posterior IPS was responding to number of items. This region showed larger responses to the two-item tasks (color-line, line-color and line-line) than the one-item tasks (color and line). As suggested in Xu & Chun (2006), the inferior IPS was responding to number of objects attended while the superior IPS was responding to number of features held in working memory. The left ventral posterior IPS was more lateral to the superior IPS in Xu et al's finding. The different findings in functional segregation of the IPS between our study and their study could be due to task differences: we used simple feature while they used both simple and multiple features. In our study, the number of feature was equal as the number of object. This could explain why the cluster that related with number of items in our study was close to the cluster which responded to number of features in Xu et al's study. We found a few clusters in posterior parietal cortex were responding to orientation than color in our study. While in their study, since they did not compare different features, they could not claim which region is sensitive to one feature over the other. In addition, as the complex feature in their study consisted of multiple features, the activation in superior IPS might reflect the issue (such as feature binding) other than number of features. That is not the focus of the current study.

The two SPL clusters were closed to the SPL reported in another visual working memory study (Song & Jiang, 2006). They found the SPL responded to both number of items and feature. Different from theirs, in our current study, the SPL showed greater responses when remembering two lines than remembering one color and one line. It suggested that this region was not purely adjusted by number of items. The discrepancy could be due to the task differences. In Song & Jiang's study, different features to be remembered were from the same object. It is possible that the participant processed both features while told to focus on one of them. While in the current study, the features to be remembered were from different objects. So if one region was sensitive to one feature than the other, we would see heightened activations when remembering one feature than the other one.

Besides posterior parietal cortex, the frontal cortex showed some functional segregation. The left dorsal PFC was responding to remembering orientation than remembering color while the left PrCG was responding to number of items. In the two clusters (the left ventral posterior IPS and PrCG), the line-line condition was numerically greater than color-line or line-color condition. It suggested these regions may serve multiple functions: representing number of items as well as maintaining orientation.

5.3 Representing item from the same category vs different categories

Studies of monkeys have shown that activity of both IT neurons and PFC neurons are altered by adding a second item when viewing or remembering one visual object (Zoccolan et al, 2005; Warden & Miller, 2007). When adding a line item into working memory, activities in SPL, IPS and dorsal PFC increased. And the increment was larger in within-category condition than in cross-category condition. When comparing remembering two orientations with remembering one color and one orientation, we found greater activation for the line-line condition in the bilateral dorsal PFC, IPS, SPL, MTG and right PrCS. One might argue that these activations could be due to orientation working memory as oppose to interference as there were more orientations in the line-line condition than in the color-line or line-color condition. This might be true but could not be the sole reason. One piece of evidence was from the ROIs' data. If one region was predominantly sensitive to orientation working memory, the activation during delay stage for color condition would be lower than the condition involving orientation. The right PrCS cluster showed greater activation in line-line condition than all the other conditions. However, one color condition was not significantly lower than one line condition or color-line condition during the delay stage. Another piece of evidence was from the contrast between two-items and one-item working memory task. We found greater enhancement in right dorsal PFC and IPS when adding a line into working memory in within-category condition than in cross-category condition. As the line item was added in both conditions, the activations differences between two conditions could not be due to orientation working memory. It suggested that higher activity in the line-line condition than in the color-line or line-color condition is probably due to and beyond simple holding orientation information in working memory.

It has been shown that a network of prefrontal-parietal regions including the posterior parietal cortex and the dorsal PFC are involved in maintaining visual spatial information (Courtney et al, 1998; Leung, Gore, & Goldman-Rakic, 2002; Leung et al, 2004; Rowe & Passingham, 2001), updating visual spatial information (Leung, Oh, Ferri,

& Yi, 2007) and resolving interference for spatial information (Leung & Zhang, 2004). The posterior parietal cortex especially the IPS was involved in representing multiple visual items (Todd & Marois, 2004; Xu & Chun, 2006). In the current study, items from the cross-category condition were better remembered than from the within-category condition. Consistent with behavioral findings, adding an item to working memory recruited a network of frontal-parietal regions and greater enhancement was observed when remembering two-items from the same category than from different categories. It could reflect larger interference between items when they are from the same category than from different categories.

5.4 Color and orientation circuit

Many researchers have compared spatial and non-spatial information processing in working memory (Mecklinger & Müller, 1996; Munk et al, 2002; Postle & D'Esposito, 1999; Smith et al, 1995) but few directly compared color and orientation information processing (Mohr et al, 2006).

In the current study, medial visual cortex and lingual gyrus were more dominant in the color condition while the Bilateral dorsal PFC, SPL, IPS, PrCG, left MTG, precuneus and right ITG were more dominant in the orientation condition. Consistent with previous findings, the lingual gyrus has been found to be involved in color perception (Clark et al, 1997; Lueck et al, 1989; Sakai et al, 1995; Zeki et al 1991). The orientation information processing was associated with more dorsal brain regions. These regions overlap with what has been found for orientation working memory (Cornette, Dupont, Bormans et al, 2001; Cornette, Dupont, Salmon et al, 2001; Cornette et al, 2002).

The lingual gyrus showed higher activity in one color condition than in one line condition. However the difference was mainly showed during the encoding stage but not the delay stage. To further examine whether any regions was shower greater activity for the color than for the orientation, we extracted ROI data from two clusters which showed stronger activation for the color than for the orientation in previous working memory study (left IFS: MNI coordinates -40 29 16; right MOG: MNI coordinates 27 -84 -3 from Mohr et al, 2006). However, activity in these regions during the one color condition was not higher than in one line condition.

In sum, there were dissociated pathways for processing color and orientation information and it was consistent with previous findings.

5.5 Limits

One potential problem of the current study is that there is perceptual difference between color and line stimulus. The shapes of these two objects were different and the area was larger for the color than the line item. This might cause some of the activation differences during encoding stage. In previous studies, some researchers tested the features within the same object (Mohr et al, 2006; Postle & D'Esposito, 1999; Song & Jiang, 2006). The participants were required to focus one feature during memory task. However, the disadvantage of such approach was that the participant might encode task-irrelevant feature and it could confound the activation (Rainer, Asaad & Miller, 1998; Rao, Rainer & Miller, 1997). While in the current study, we avoid such confound.

In the behavioral study, in order to examine the individual items, we presented cue at the probe stage. However, the cue with negative probe was not informative as the negative probe did not match any remembered stimulus. The participant could still make a correct judgment even when they did not pay attention to the cue. One possible solution is presenting the remembered stimuli at different locations so that the participants know which one to compare. In our pilot study, we presented stimuli peripherally as well as in the center. The performance pattern was similar and we observed higher recognition rate and faster response time in cross-category condition than in within-category condition. So in the future we should do a follow up study with memory stimuli presented peripherally. Another solution is we could let some negative probes match the one which they are not supposed to compare with. However it would induce interference at the probe stage. And this is not what we want at the current stage.

The behavioral differences between within-category condition and cross-category condition was not too large, especially in fMRI study, the accuracy difference was marginally significant. One possible reason was that the task was so easy that it cannot differentiate within-category and cross-category condition. Another reason could hold us from seeing the larger performance differences between within-category condition and cross-category condition was the transition between categories. In the cross-category condition, the two stimuli were from different categories. If they are represented in different neural circuit, the participant might have to shift attention between them when holding both items. The shifting cost might cancel some of the facilitation effect when remembering items from different categories.

The fMRI measures the haemodynamic response. The signal is dependent on the blood oxygen level (BOLD signal). As neural activity increases, the consumption of oxygen increases, which results in the increase of the BOLD signal. As it takes time for the BOLD signal to reach peak, the temporal resolution of fMRI was very low. So in fMRI studies, we have to use relative longer interval between items (In the current study, the delay was set at 8.3s and the ITI was set at 9.5sec or longer). Though the delay was set at 8.3 sec, the haemodynamic response of stimuli encoding might still affect the activities during the delay stage. On the other hand, the activity during the encoding stage reflected not purely encoding process. It may involve both stimulus encoding and maintenance. This could lower the activity of maintenance we observed.

6 Conclusion

Our results demonstrated that interference between items was larger when they were from the same category than when they were from different categories. When adding a line to working memory, a network of frontal-parietal regions was recruited including the dorsal prefrontal cortex and posterior parietal cortex. Particularly, the right IPS and dorsal PFC showed greater enhancement in within-category condition than in cross-category condition. Posterior parietal cortex are functional segregated with the bilateral IPS and SPL involved in representing orientation and the left posterior IPS involved in representing number of items. The regions which showed greater activities in within-category condition than in cross-category condition could be involved in resolving interference between items.

Tables and Figures

Table 1 Regions Involved in Color and Orientation Information Processing

contrast	region	Coordinates			Main effect (p)
		x	y	z	
Color vs orientation	L. LG	15	-66	-3	n.s
	R. LG	-3	-84	6	n.s
Orientation vs color	L. dPFC	-24	-12	48	***
	L. SPL	-21	-63	48	***
	L. IPS	-45	-36	39	***
	L. Pcu	-9	-72	57	***
	R. IPS	21	-75	51	***
	R. SPL	27	-60	48	***
	L. MTG	-54	-48	-3	p =.058
	R. ITG	51	-57	-6	***
	R dPFC	36	-12	45	**
	R. PrCG	54	9	24	***
	L. PrCG	-57	3	30	***
Color & orientation	R. fusiform	33	-66	-6	n.s.
	L. fusiform	-24	-81	-18	*
	L. IPS	-30	-66	39	***
	L. IPS	-36	-51	33	***
	preSMA	3	15	48	*
	SMA	-3	-3	54	n.s.
	L. PrCS	-48	-12	48	n.s.
	R. insular	36	24	0	n.s
	R. MFG	30	45	18	n.s

These regions showed supra-threshold activity during encoding+delay epochs ($p < .05$, FDR corrected). Main effect column showed the p values of one way ANOVA of the five task conditions at the delay stage (n.s: $p > .1$ * $p < .05$, ** $p < .01$, *** $p < .001$). Abbreviations: ITG: inferior temporal gyrus; SPL: superior parietal lobe; IPS: intraparietal sulcus; LG: lingual gyrus; MFG: middle frontal gyrus; MTG: middle temporal gyrus; Pcu: precuneus; PrCG: precentral gyrus; preSMA: pre-supplementary motor area; SMA: supplementary motor area; L: left; R. right.

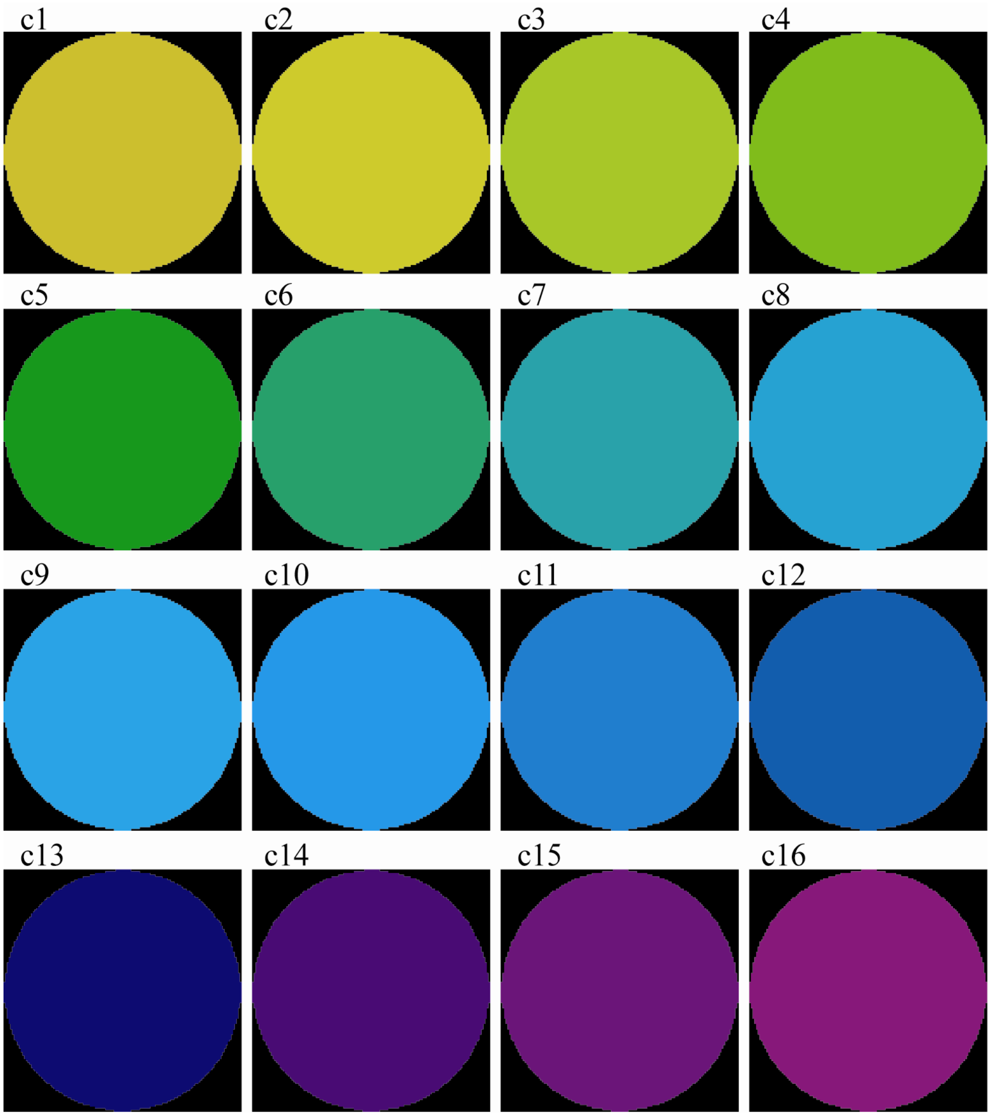

Figure 1
Color stimuli used in the experiments. There were 16 stimuli. The colors only varied in hue and were controlled for luminance and saturation parameters.

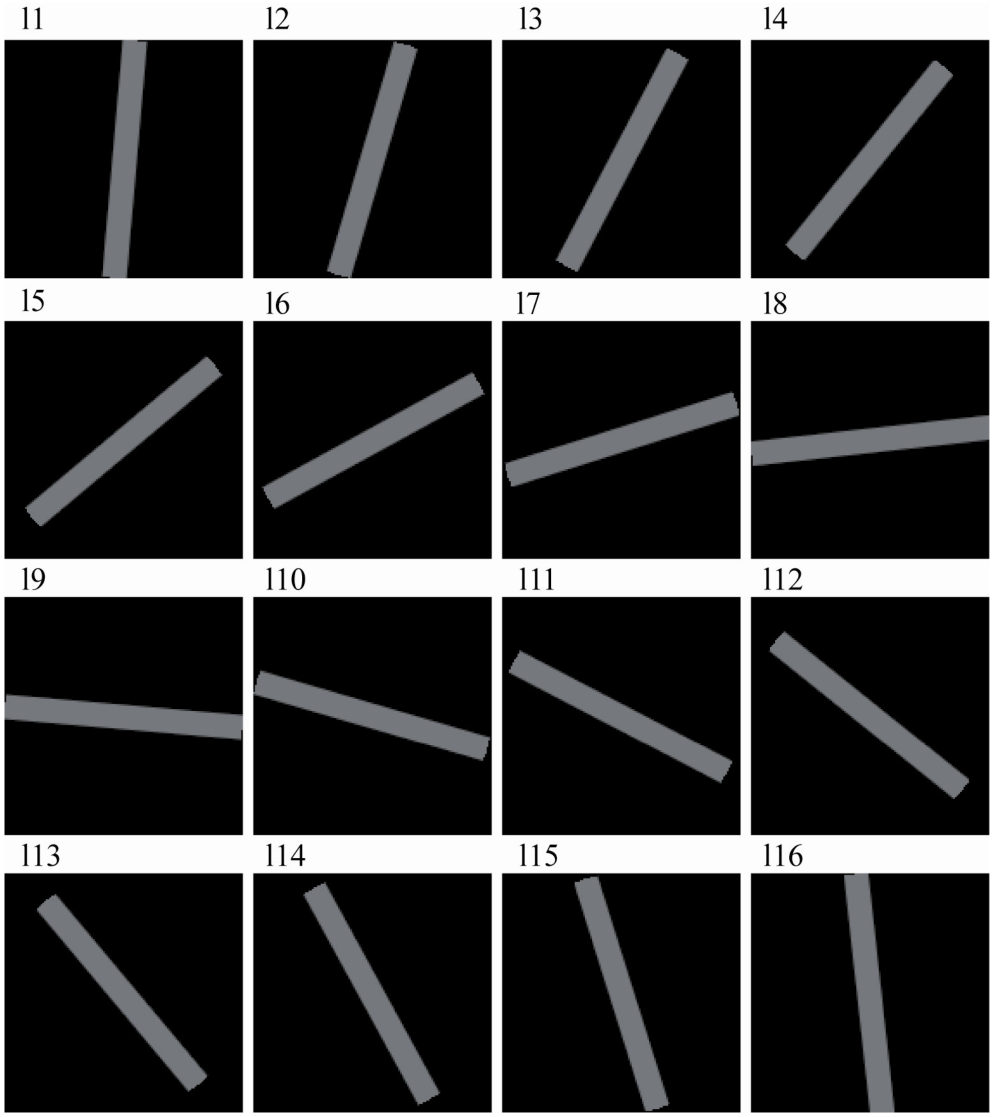

Figure 2
Line orientation stimuli used in the experiments. There were 16 stimuli. The two adjacent orientations were separated by 11.25 deg.

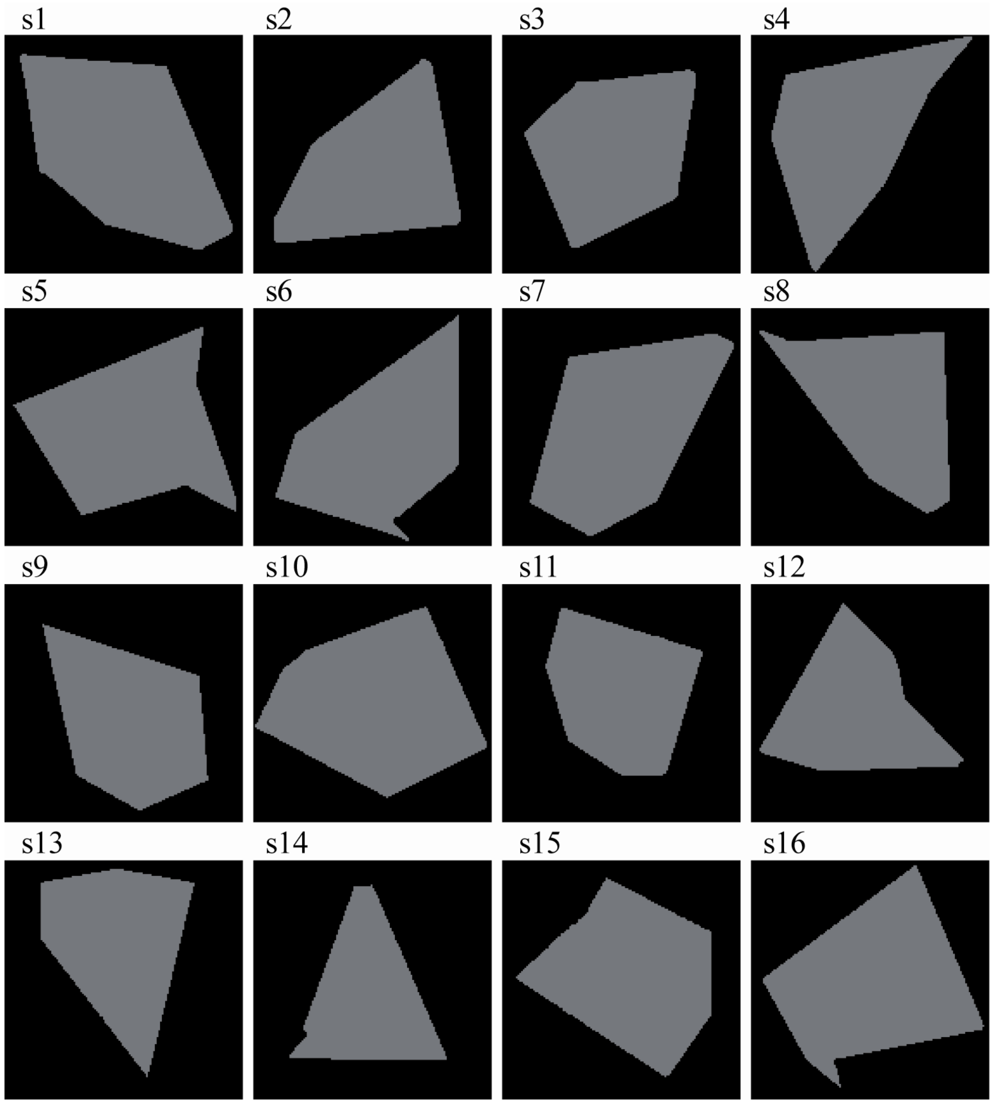

Figure 3
Shape stimuli used in the experiments. There were 16 Attneave shapes (Attneave and Arnoult, 1956).

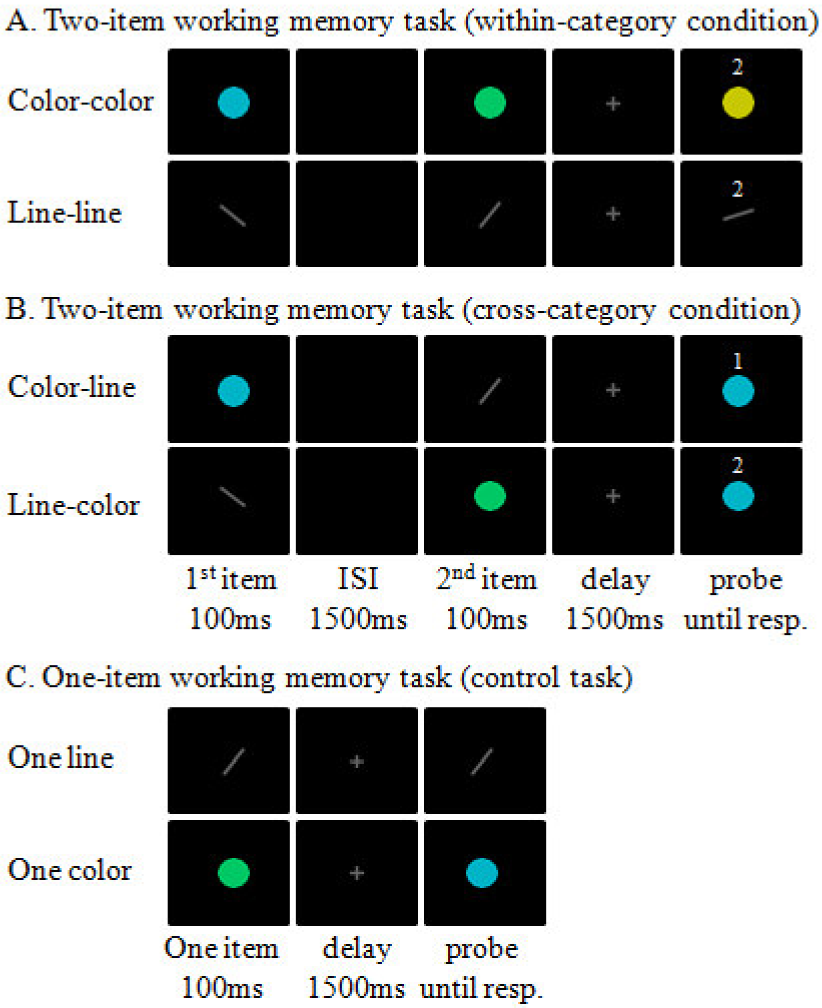

Figure 4
Paradigm of Experiment 1 (Comparison between the Within-category and the Cross-category Condition). (A) & (B) A sequence of trial events during the two-item working memory task in experiment 1a and 1b. A memory set of two items were presented sequentially followed by a delay and then a probe.. The probe stayed on the screen until the participant made a response. There were two types of task conditions: within-category condition (color-color or line-line) and cross-category condition (color-line or line-color). In experiment 1a, participants had to remember both items. At the probe stage, the stimulus was presented in the center with a cue above it. If the cue was 1, they had to compare the probe with the first item. If the cue was 2, they had to compare the probe with the second item. In experiment 1b, participants only need to remember one item and ignore the other. There was no cue above the stimulus at the probe stage. Refer to the text for the timing of each event. (C) Sequence of trials events during the one-item working memory task in experiment 1a and 1b. Only one item was presented for the later recognition test. There were two task conditions: one color and one line.

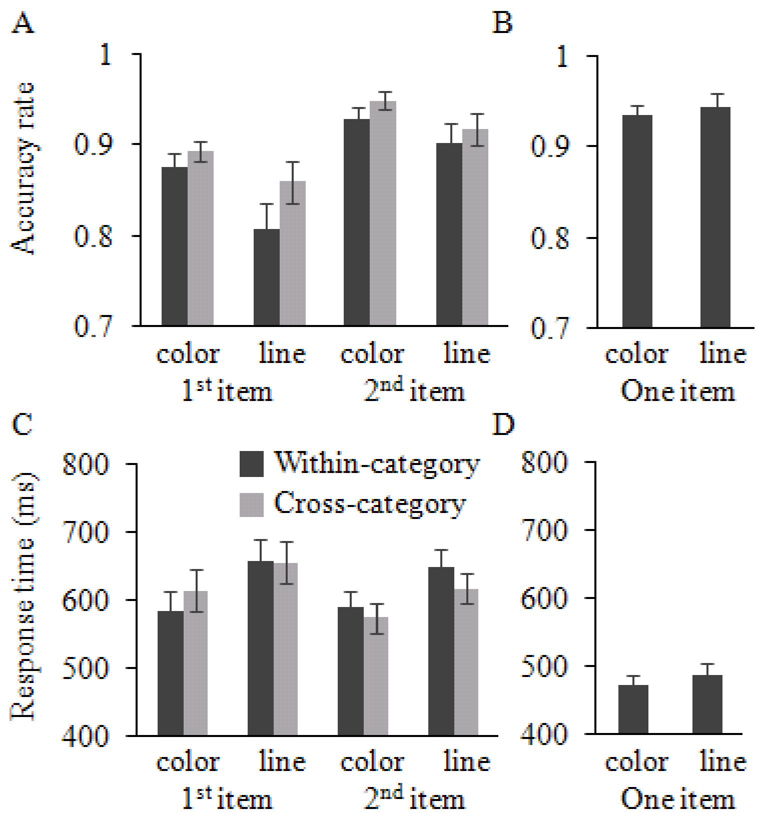

Figure 5
Results from exp1A (Comparison between the Within-category and the Cross-category Condition). Data were presented according to probe and condition. Error bars shows the standard error.
A: accuracy data from the two-item working memory task
B: accuracy data from the one-item working memory task
C: response time data from the two-item working memory task
D: response time data from the one-item working memory task

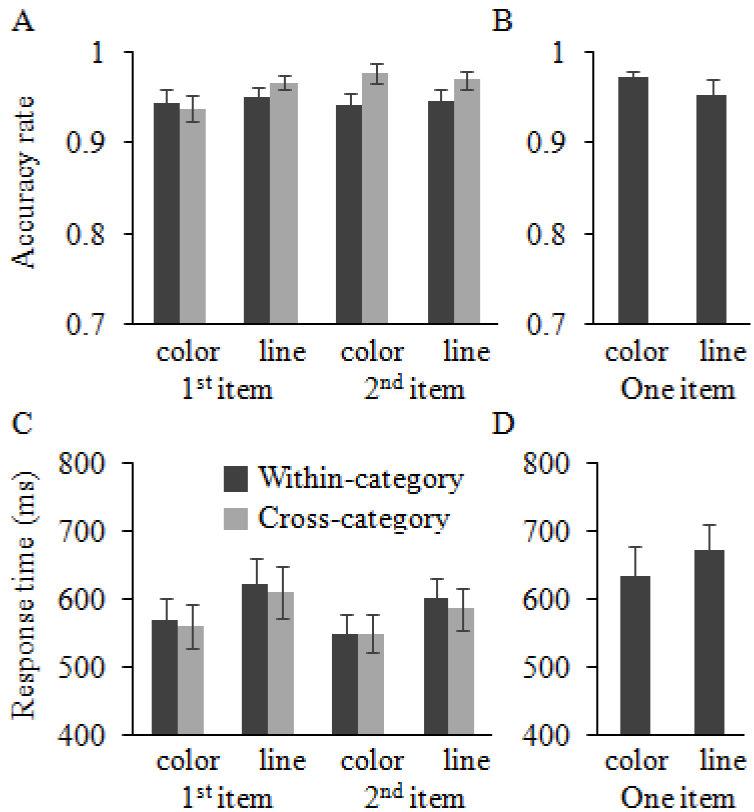

Figure 6
Results from exp1B (Comparison between the Within-category and the Cross-category Condition: perceptual interference control). Data were presented according to the probe feature and condition (first item refers to only remembering the first item; second item refers to remembering the second item). Error bars reflect the standard error.
A: accuracy data from the two-item working memory task
B: accuracy data from the one-item working memory task
C: response time data from the two-item working memory task
D: response time data from the one-item working memory task

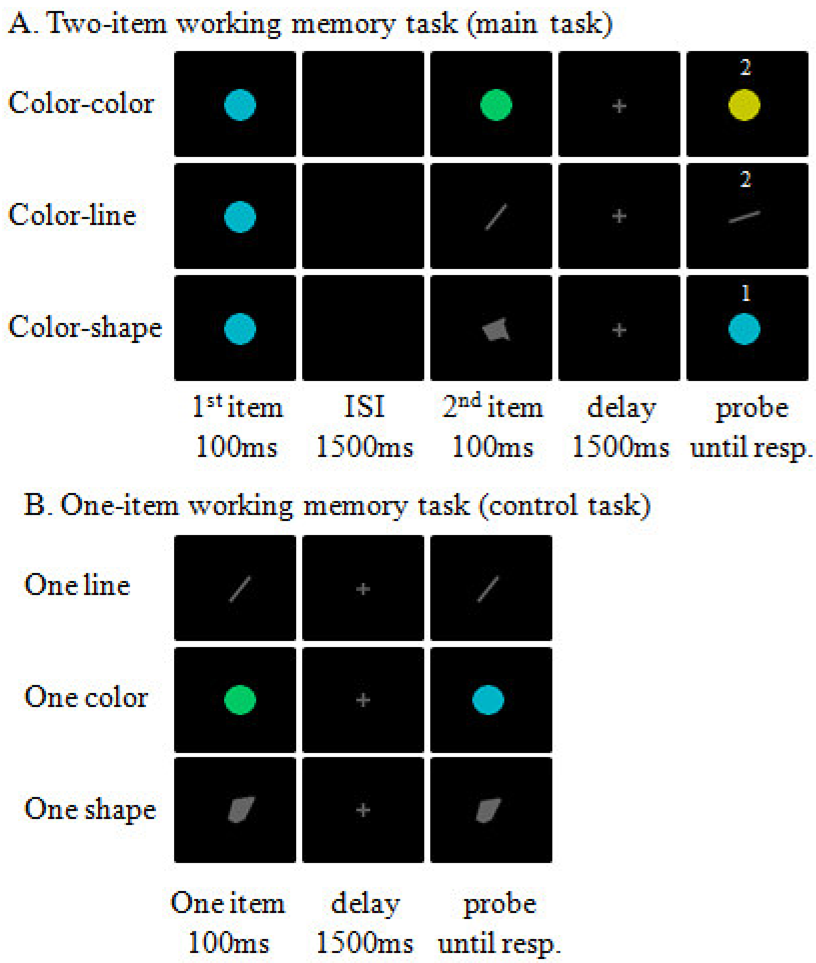

Figure 7
Paradigm of experiment 2 (Effect of Existing Working Memory on Encoding and Maintaining a New Item). (A) A sequence of trial events during the two-item working memory task in experiment 2. A memory set of two items were presented sequentially followed by a delay and then a probe. The probe stayed on the screen until the participant made a response. There were three task conditions: color-color, color-line and color shape. Participants had to remember both items. At the probe stage, the stimulus was presented in the center with a cue above it. If the cue was 1, they had to compare the probe with the first item. If the cue was 2, they had to compare the probe with the second item. (B) Sequence of trials events during the one-item working memory task in experiment 2. Only one item was presented for later recognition test. There were three task conditions: one color, one line and one shape.

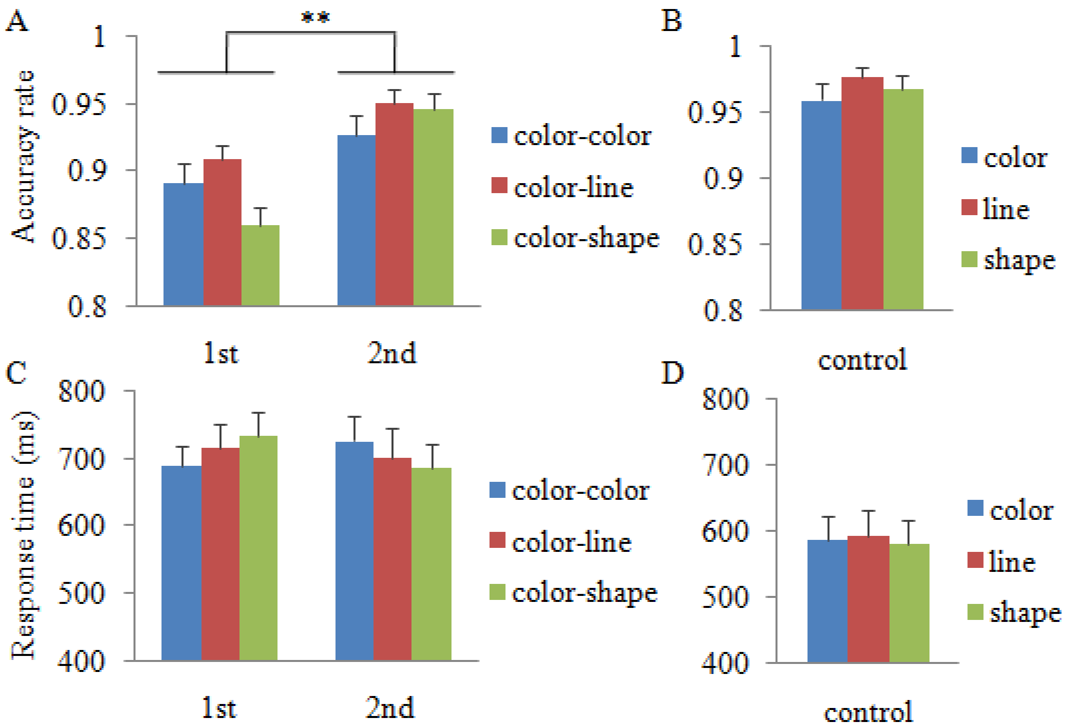

Figure 8

Results from experiment 2 (Effect of Existing Working Memory on Encoding and Maintaining a New Item). Error bars reflect the standard error. Statistical differences were marked (** p<.01).

A. Accuracy of the two-item working memory task in experiment 2. There are three task conditions (color-color, color-line and color-shape). 1st and 2nd refer to the 1st and 2nd item of the remembered items.

B. Accuracy of the one-item working memory task in experiment 2. There are three tasks conditions (color, line and shape). Control means the one-item working memory task.

C. RT of the two-item working memory task in experiment 2. There are three task conditions (color-color, color-line and color-shape). 1st and 2nd refer to the 1st and 2nd item of the remembered items.

D. RT of the one-item working memory task in experiment 2. There are three tasks conditions (color, line and shape). Control means the one-item working memory task.

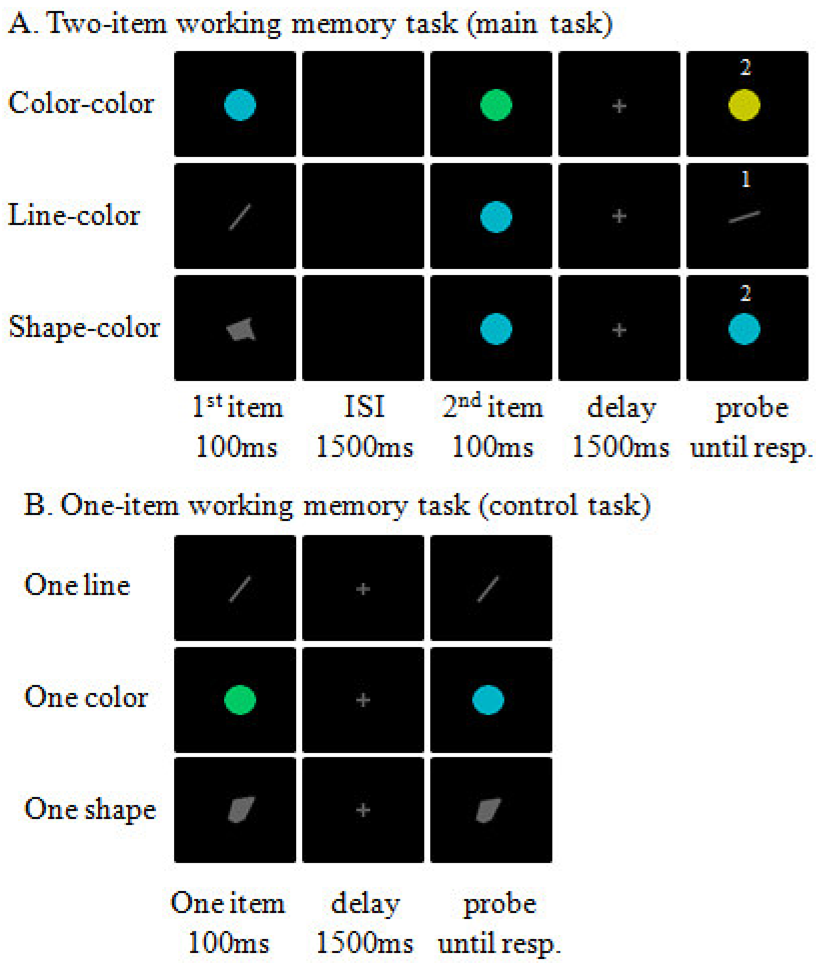

Figure 9
Paradigm of experiment 3 (Effect of Encoding and Maintaining a New Item on Existing Working Memory). (A) A sequence of trial events during the two-item working memory task in experiment 3. A memory set of two items were presented sequentially followed by a delay and then a probe. Refer to the text for the timing of each event. The probe stayed on the screen until the participant made a response. There were three task conditions: color-color, line-color and shape-color. Participants had to remember both items. At the probe stage, the stimulus was presented in the center with a cue above it. If the cue was 1, they had to compare the probe with the first item. If the cue was 2, they had to compare the probe with the second item. (B) Sequence of trials events during the one-item working memory task in experiment 2. Only one item was presented before the delay period. There were three task conditions: one color, one line and one shape.

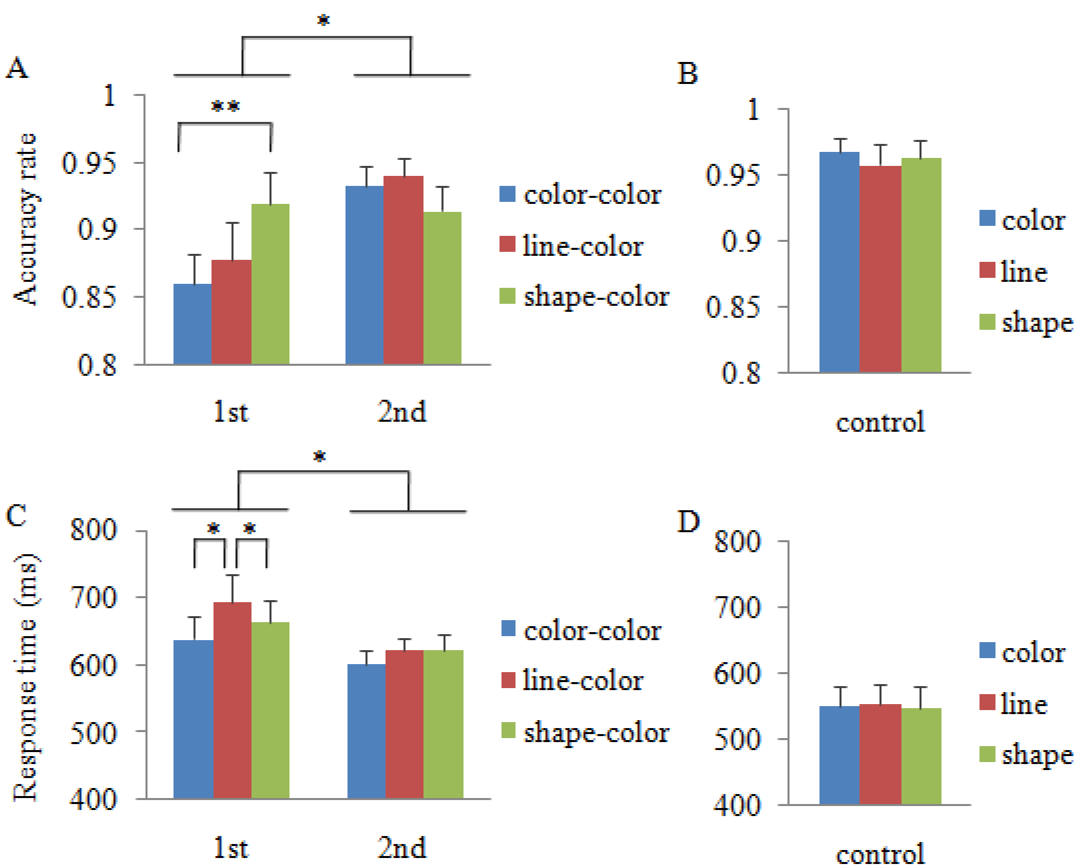

Figure 10
Results from experiment 3 (Effect of Encoding and Maintaining a New Item on Existing Working Memory). Error bars reflect the standard error under that condition. Statistical differences were marked (* $p< .05$, ** $p<.01$).
A. Accuracy of the two-item working memory task in experiment 3. There are three task conditions (color-color, line-color and shape-color). 1st and 2nd refer to the 1st and 2nd item of the remembered items.
B. Accuracy of the one-item working memory task in experiment 3. There are three tasks conditions (color, line and shape). Control means the one-item working memory task.
C. RT of the two-item working memory task in experiment 3. There are three task conditions (color-color, line-color and shape-color). 1st and 2nd refer to the 1st and 2nd item of the remembered items.
D. RT of the one-item working memory task in experiment 3. There are three tasks conditions (color, line and shape). Control means the one-item working memory task.

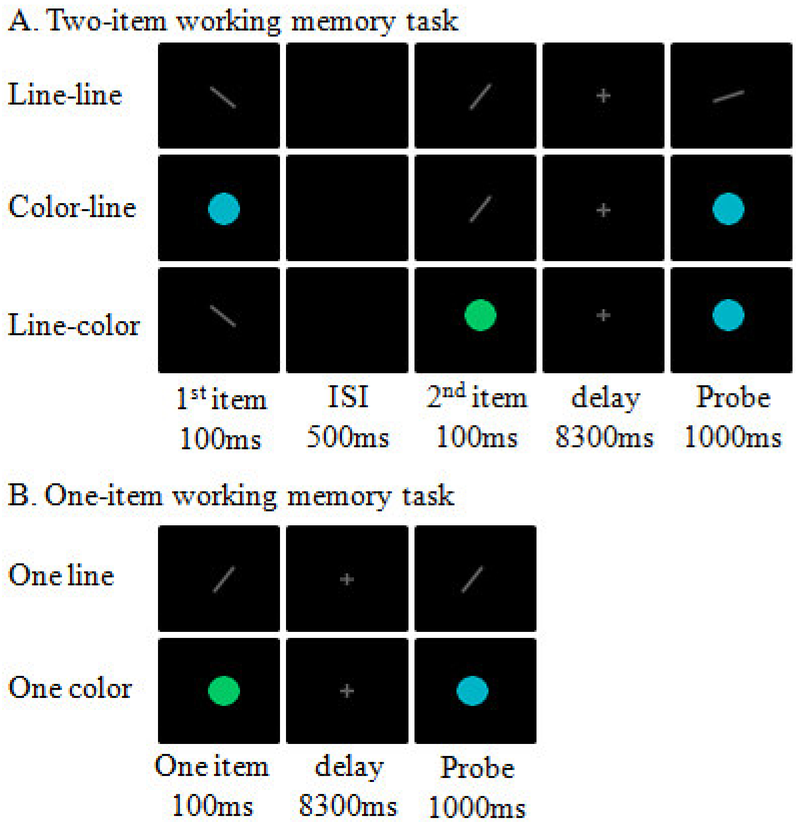

Figure 11
Paradigm of experiment 4A and 4B (Multiple Item Working Memory: an fMRI Experiment). (A) A sequence of trial events during the two-item working memory task in experiment 4A and 4B. A memory set of two items were presented sequentially followed by a delay and then a probe. There were three task conditions: line-line color-line and line-color). Participants had to remember both items. (B) Sequence of trials events during the one-item working memory task in experiment 4A and 4B. Only one item was presented before the delay period. There were two task conditions: one color and one line. Refer to the text for the timing of each event of experiment 4B (fMRI experiment).

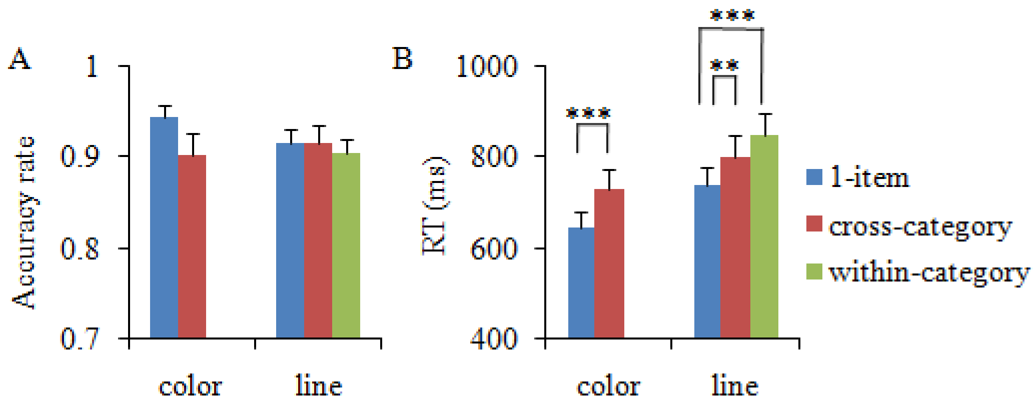

Figure 12
Results from experiment 4A (Multiple Item Working Memory: an fMRI Experiment – Outside the Scanner). The results are presented by the probe type (color & line) and task condition (one-item, cross-category and within-category). Both cross-category and within-category belong to two-item working memory tasks. Error bars reflect the standard error. Statistical differences were marked (** $p< .01$, *** $p<.001$).
(A) accuracy of experiment 4A. (B) response time of experiment 4A

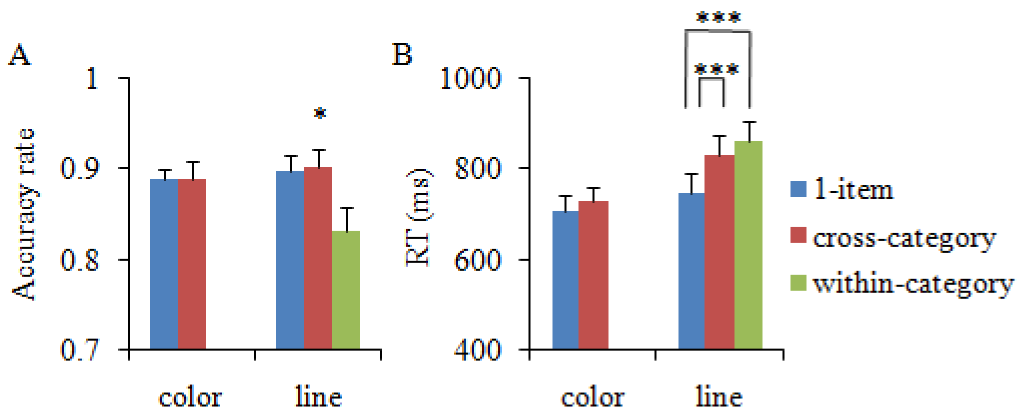

Figure 13
Behavioral results from experiment 4B (Multiple Item Working Memory: an fMRI Experiment – Inside the Scanner). The results are presented by the probe type (color & line) and task condition (one-item, cross-category and within-category). Both cross-category and within-category belong to the two-item working memory tasks. Error bars reflect the standard error. Statistical differences were marked (* p< .05, *** p<.001). (A) accuracy of experiment 4B. (B) response time of experiment 4B

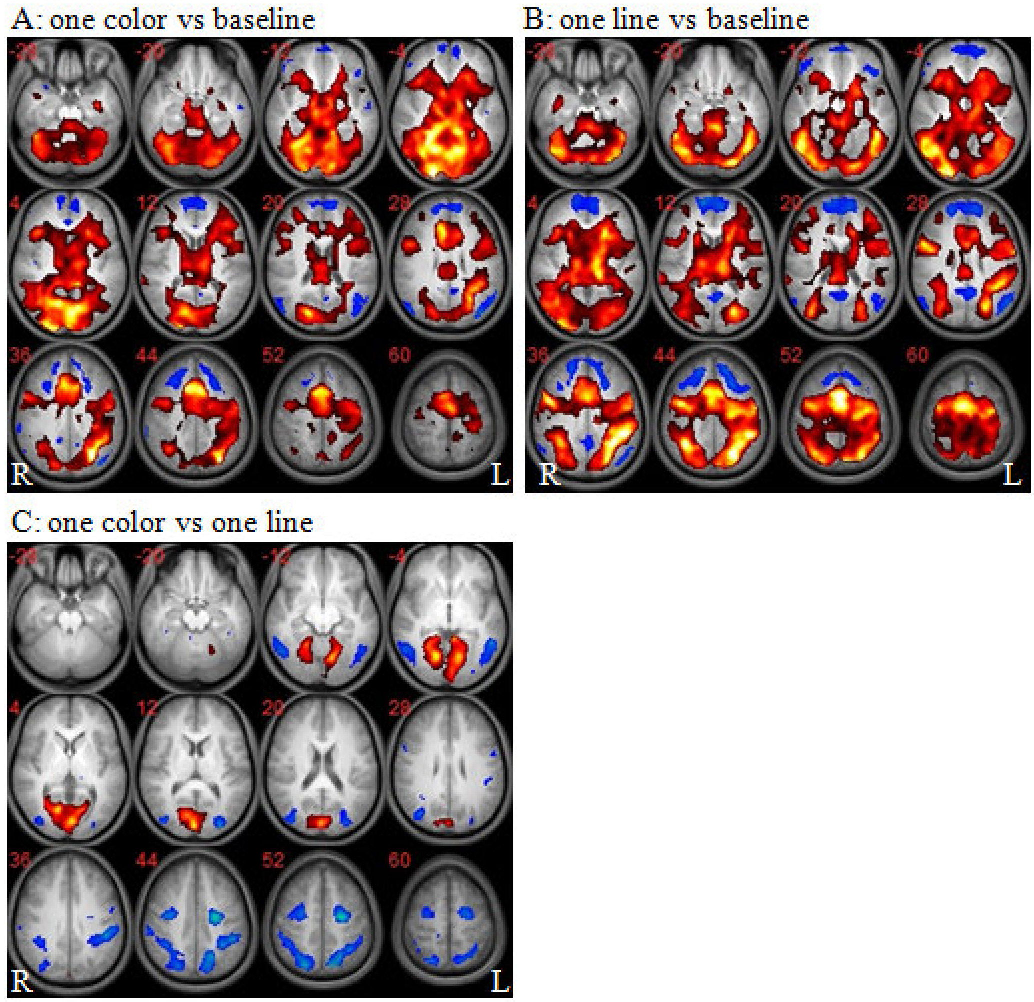

Figure 14
Group activation results of the encoding+delay stage for the 1-item conditions ($p < .05$, FDR corrected, cluster size > =9). Left side on the figure is the right side of the brain. (A) color vs baseline (B) line vs baseline (C) color vs line

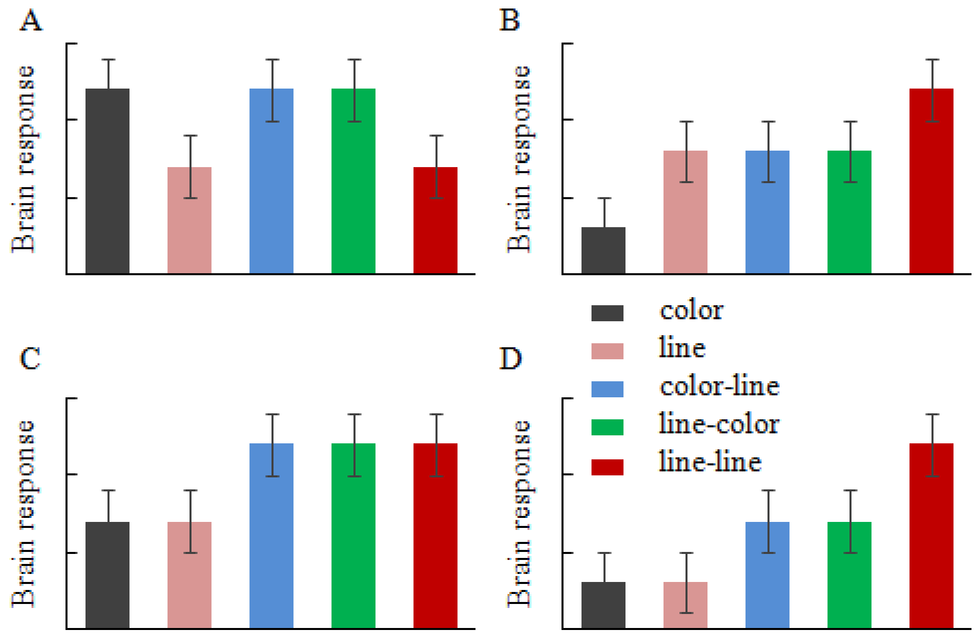

Figure 15
Predict patterns of fMRI signals
X-axis shows the task conditions.
Y-axis represents the hypothetical level of brain response for each condition
A: region show selective activity to color
B: region show selective activity to line
C: region show selective activity to number of items
D: region show selective activity to within-category condition than cross-category condition

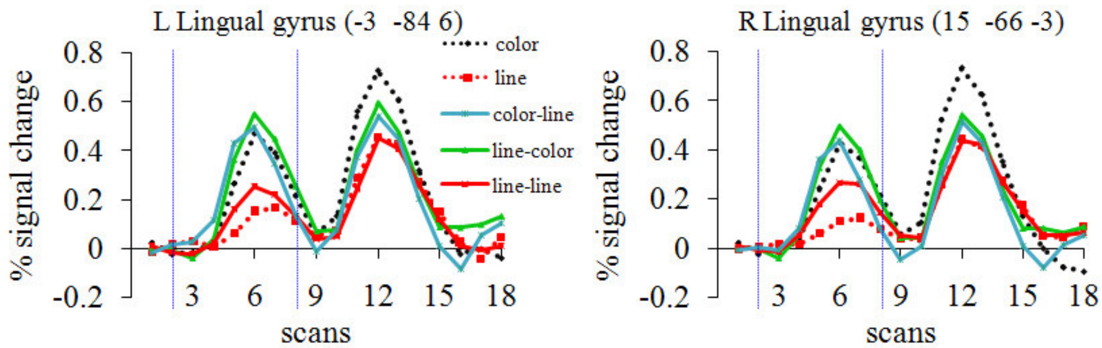

Figure 16
Time courses of the regions showed greater activation for color than orientation. Two vertical lines indicate the onset of delay and onset of probe

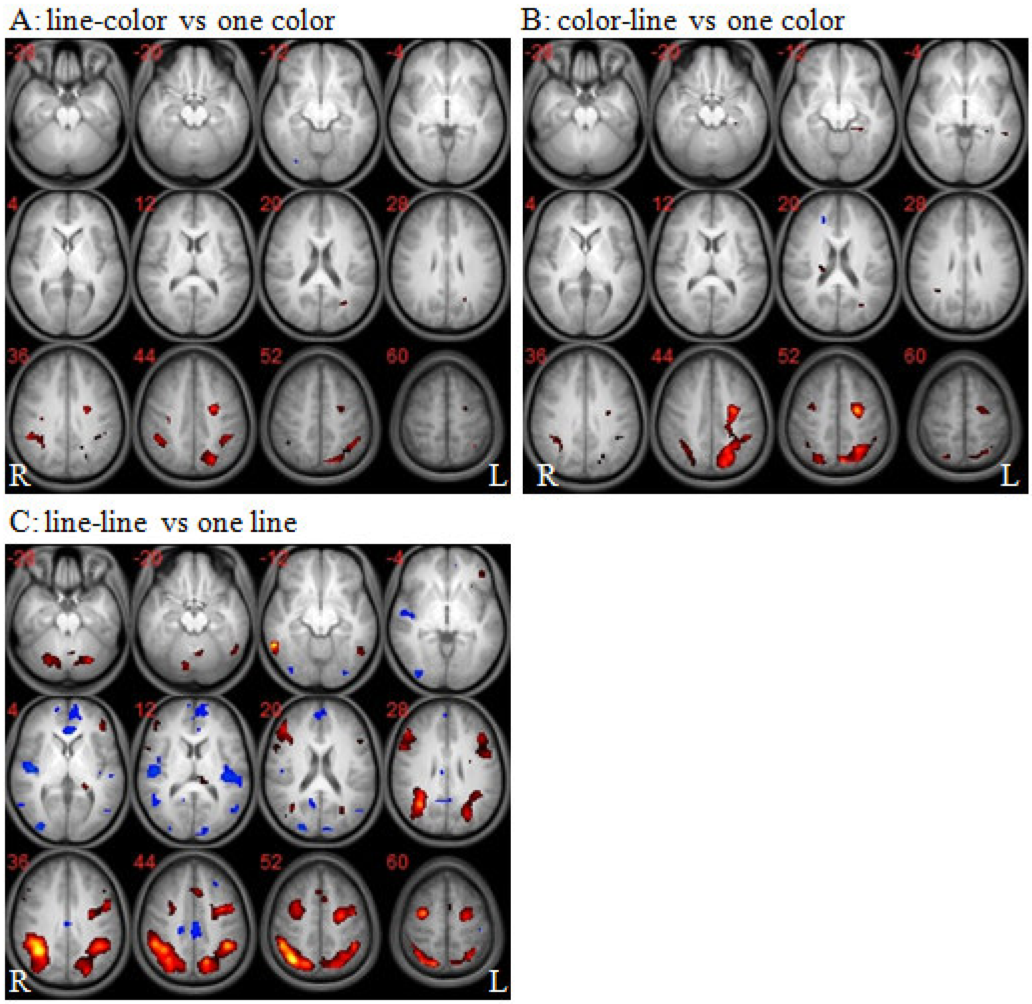

Figure 17
Group activation results of the delay stage ($p < .05$, FDR corrected, cluster size > =9). Left side on the figure is the right side of the brain. (A) line-color vs one color (B) color-line vs one color (C) line-line vs one line

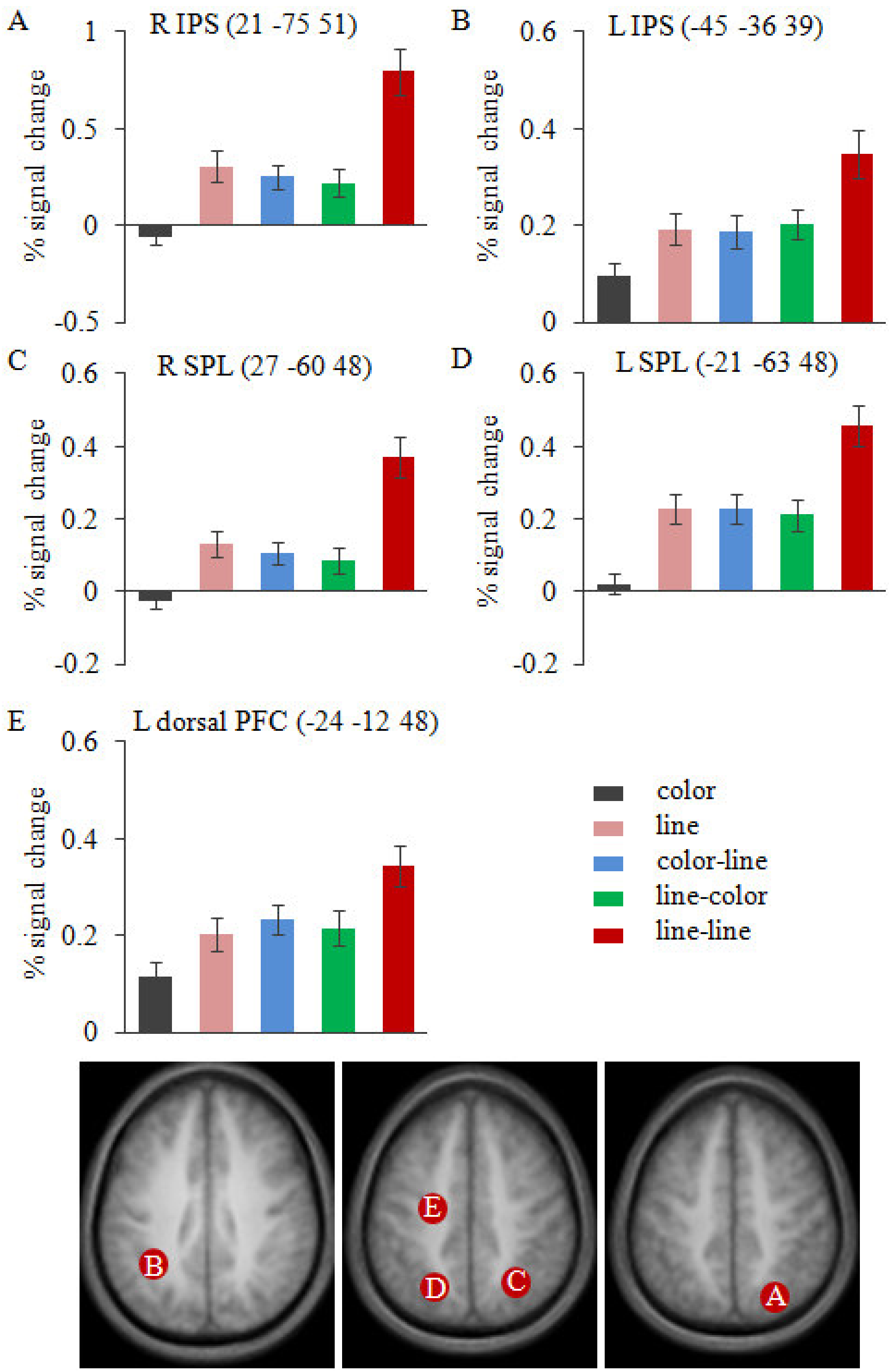

Figure 18
Level of activation during the delay stage under different conditions is shown for selected ROIs. Error bars reflect the standard error under that condition.
These regions showed greater activity in response to the orientation than color stimuli. Bottom figures show the cluster locations (Left side on the figure is the right side of the brain)

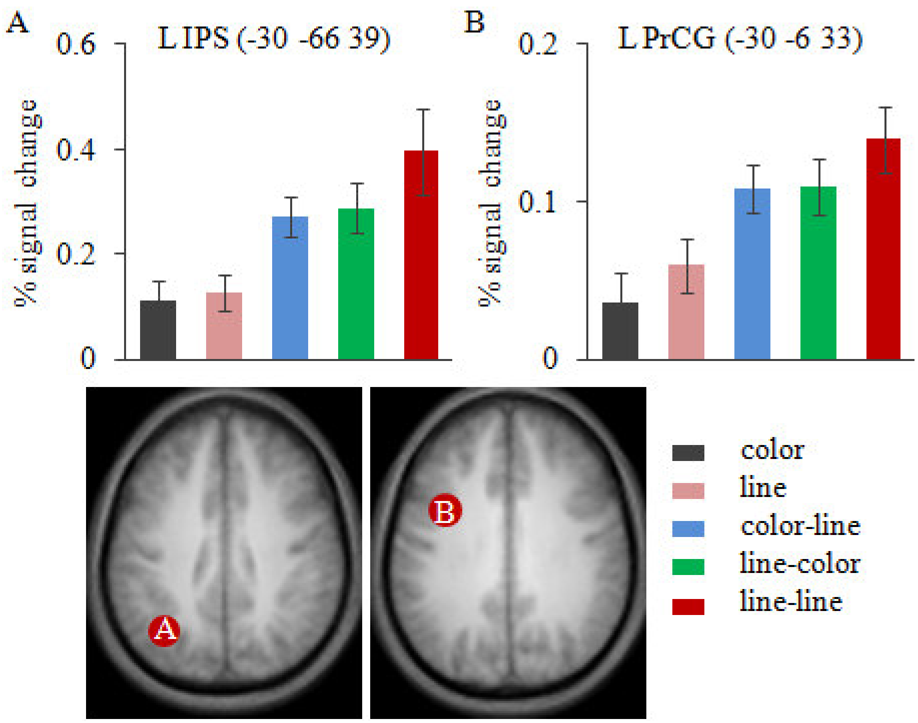

Figure 19
Level of activation during the delay stage under different conditions is shown for selected ROIs. Error bars reflect the standard error.
These regions showed greater activity when remembering two-items than remembering one item regardless of feature. The bottom figure show the cluster locations (Left side on the figure is the left side of the brain)

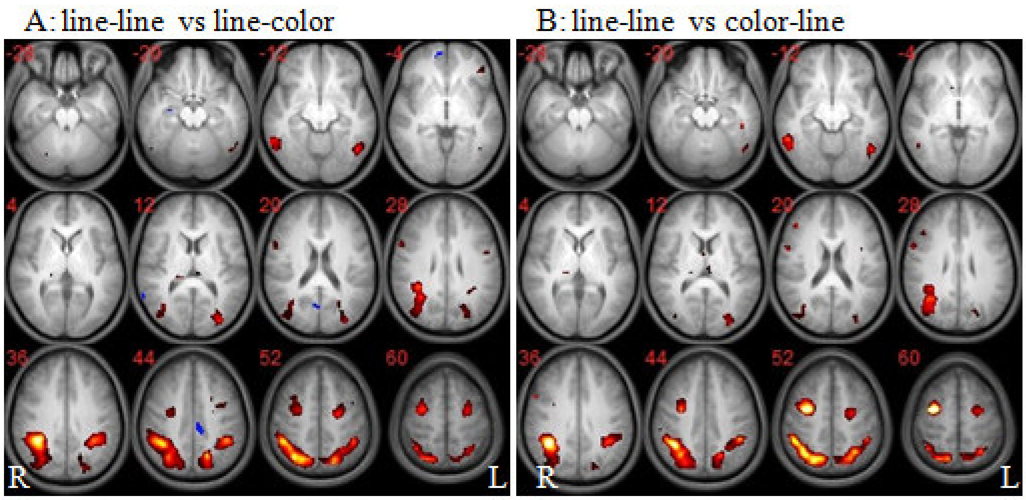

Figure 20
Group activation results of the delay stage (p < .05, FDR corrected, cluster size > =9). Left side on the figure is the right side of the brain. (A) line-line vs line-color (B) line-line vs color-line

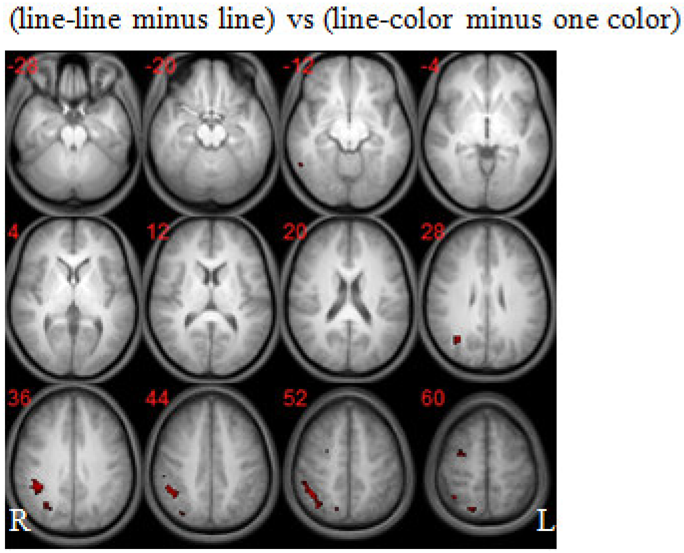

Figure 21

Group activation results of the delay stage. Left side on the figure is the right side of the brain. This figure shows (line-line minus line) vs (line-color minus one color) ($p < .001$, uncorrected, cluster size > =9)

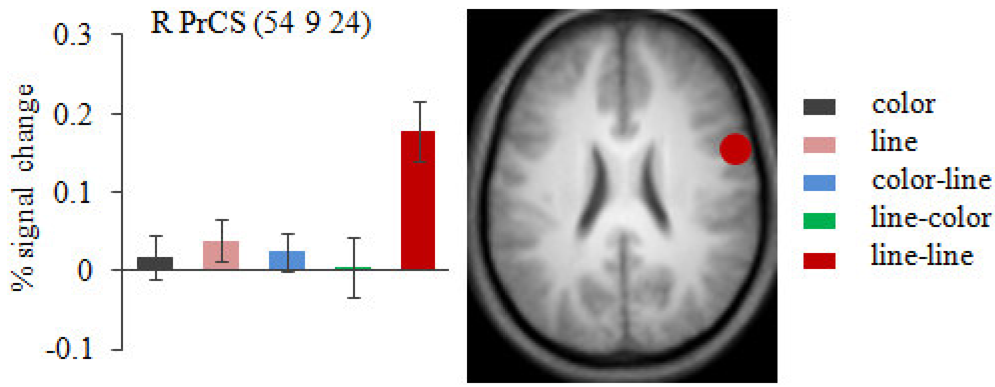

Figure 22
Level of activation during the delay stage under different conditions is shown for selected ROIs. Error bars reflect the standard error.
This region showed stronger activity in the within-category condition than in the cross-category condition. The right figure shows the cluster locations (Left side on the figure is the left side of the brain)

References

Alvarez, G. A., & Cavanagh, P. (2004). The capacity of visual short-term memory is set both by visual information load and by number of objects. *Psychol Sci, 15*(2), 106-111.

Amit, D. J., Bernacchia, A., & Yakovlev, V. (2003). Multiple-object working memory--a model for behavioral performance. *Cereb Cortex, 13*(5), 435-443.

Atkinson, R. C., & Shiffrin, R. M. (1968). Human memory: A proposed system and its control processes. In K. W. Spence & J. T. Spence (Eds.), *The psychology of learning and motivation* (Vol. 2, pp. 89-195). New York: Academic Press.

Baddeley, A. (1986). *Working memory*. New York, NY, US: Clarendon Press/Oxford University Press.

Bentin, S., Allison, T., Puce, A., & Perez, E. (1996). Electrophysiological studies of face perception in humans. *Journal of Cognitive Neuroscience, 8*(6), 551-565.

Berdyyeva, T. K., & Olson, C. R. (2009). Monkey supplementary eye field neurons signal the ordinal position of both actions and objects. *J Neurosci*, 29(3), 591-599.

Bosch, V., Mecklinger, A., & Friederici, A. D. (2001). Slow cortical potentials during retention of object, spatial, and verbal information. *Brain Res Cogn Brain Res, 10*(3), 219-237.

Broadbent, D. E., Broadbent, D. E., & Broadbent, M. H. (1981). Recency effects in visual memory. *The Quarterly Journal of Experimental Psychology A: Human Experimental Psychology*, *33A*, 1-15

Brown, J., & Brown, J. (1958). Some tests of the decay theory of immediate memory. *The Quarterly Journal of Experimental Psychology, 10*, 12-21.

Busch, N. A., & Herrmann, C. S. (2003). Object-load and feature-load modulate EEG in a short-term memory task. *Neuroreport, 14*(13), 1721-1724.

Callicott, J. H., Mattay, V. S., Bertolino, A., Finn, K., Coppola, R., Frank, J. A., Goldberg, T. E., & Weinberger, D. R. (1999). Physiological characteristics of capacity constraints in working memory as revealed by functional MRI. *Cereb Cortex, 9*(1), 20-26.

Chao, L. L., & Knight, R. T. (1995). Human prefrontal lesions increase distractibility to irrelevant sensory inputs. *Neuroreport, 6*(12), 1605-1610.

Chao, L. L., & Knight, R. T. (1998). Contribution of human prefrontal cortex to delay performance. *J Cogn Neurosci, 10*(2), 167-177.

Claeys, K. G., Dupont, P., Cornette, L., Sunaert, S., Van Hecke, P., De Schutter, E., & Orban, G. A. (2004). Color discrimination involves ventral and dorsal stream visual areas. *Cereb Cortex, 14*(7), 803-822.

Clark, V. P., Parasuraman, R., Keil, K., Kulansky, R., Fannon, S., Maisog, J. M., Ungerleider, L. G., & Haxby, J. V. (1997). Selective attention to face identity and color studied with fMRI. *Human Brain Mapping, 5*(4), 293-297.

Cohen, J. D., Perlstein, W. M., Braver, T. S., Nystrom, L. E., Noll, D. C., Jonides, J., & Smith, E. E. (1997). Temporal dynamics of brain activation during a working memory task. *Nature, 386*(6625), 604-608.

Cornette, L., Dupont, P., Bormans, G., Mortelmans, L., & Orban, G. A. (2001). Separate neural correlates for the mnemonic components of successive discrimination and working memory tasks. *Cereb Cortex, 11*(1), 59-72.

Cornette, L., Dupont, P., & Orban, G. A. (2002). The neural substrate of orientation short-term memory and resistance to distractor items. *Eur J Neurosci, 15*(1), 165-175.

Cornette, L., Dupont, P., Salmon, E., & Orban, G. A. (2001). The neural substrate of orientation working memory. *J Cogn Neurosci, 13*(6), 813-828.

Courtney, S. M., Petit, L., Maisog, J. M., Ungerleider, L. G., & Haxby, J. V. (1998). An area specialized for spatial working memory in human frontal cortex. *Science, 279*(5355), 1347-1351.

Cowan, N. (2001). The magical number 4 in short-term memory: a reconsideration of mental storage capacity. *Behav Brain Sci, 24*(1), 87-114; discussion 114-185.

de Fockert, J. W., Rees, G., Frith, C. D., & Lavie, N. (2001). The role of working memory in visual selective attention. *Science, 291*(5509), 1803-1806.

Della Sala, S., Gray, C., Baddeley, A., Allamano, N., & Wilson, L. (1999). Pattern span: a tool for unwelding visuo-spatial memory. *Neuropsychologia, 37*(10), 1189-1199.

D'Esposito, M., Aguirre, G. K., Zarahn, E., Ballard, D., Shin, R. K., & Lease, J. (1998). Functional MRI studies of spatial and nonspatial working memory. *Brain Res Cogn Brain Res, 7*(1), 1-13.

Druzgal, T. J., & D'Esposito, M. (2001). Activity in fusiform face area modulated as a function of working memory load. *Brain Res Cogn Brain Res, 10*(3), 355-364.

du Boisgueheneuc, F., Levy, R., Volle, E., Seassau, M., Duffau, H., Kinkingnehun, S., Samson, Y., Zhang, S., & Dubois, B. (2006). Functions of the left superior frontal gyrus in humans: a lesion study. *Brain, 129*(Pt 12), 3315-3328.

Eng, H. Y., Chen, D., & Jiang, Y. (2005). Visual working memory for simple and complex visual stimuli. *Psychon Bull Rev, 12*(6), 1127-1133.

Epstein, R., & Kanwisher, N. (1998). A cortical representation of the local visual environment. *Nature, 392*(6676), 598-601.

Funahashi, S., Bruce, C. J., & Goldman-Rakic, P. S. (1989). Mnemonic coding of visual space in the monkey's dorsolateral prefrontal cortex. *J Neurophysiol, 61*(2), 331-349.

Gazzaley, A., Cooney, J. W., McEvoy, K., Knight, R. T., & D'Esposito, M. (2005). Top-down enhancement and suppression of the magnitude and speed of neural activity. *J Cogn Neurosci, 17*(3), 507-517.

Genovese, C. R., Lazar, N. A., & Nichols, T. (2002). Thresholding of statistical maps in functional neuroimaging using the false discovery rate. *Neuroimage*, 15(4), 870-878.

Goldberg, T. E., Berman, K. F., Randolph, C., Gold, J. M., & Weinberger, D. R. (1996). Isolating the mnemonic component in spatial delayed response: a controlled PET 15O-labeled water regional cerebral blood flow study in normal humans. *Neuroimage, 3*(1), 69-78.

Goldman-Rakic, P. (1987). Circuitry of primate prefrontal cortex and regulation of behavior by representational memory. In F. Plum (Ed.), *Handbook of Physiology, The Nervous System* (Vol. 5, pp. 373-417). Bethesda, MD: American Physiological Society.

Golob, E. J., & Starr, A. (2004). Serial position effects in auditory event-related potentials during working memory retrieval. *J Cogn Neurosci, 16*(1), 40-52.

Hillyard, S. A., & Anllo-Vento, L. (1998). Event-related brain potentials in the study of visual selective attention. *Proc Natl Acad Sci U S A, 95*(3), 781-787.

Ikeda, T., & Osaka, N. (2007). How are colors memorized in working memory? A functional magnetic resonance imaging study. *Neuroreport, 18*(2), 111-114.

Jha, A. P., Fabian, S. A., & Aguirre, G. K. (2004). The role of prefrontal cortex in resolving distractor interference. *Cogn Affect Behav Neurosci, 4*(4), 517-527.

Jiang, Y. (2004). Time window from visual images to visual short-term memory: consolidation or integration? *Exp Psychol, 51*(1), 45-51.

Jiang, Y., & Kumar, A. (2004). Visual short-term memory for two sequential arrays: one integrated representation or two separate representations? *Psychon Bull Rev, 11*(3), 495-500.

Jiang, Y., Kumar, A., & Vickery, T. J. (2005). Integrating sequential arrays in visual short-term memory. *Exp Psychol, 52*(1), 39-46.

Jiang, Y., Olson, I. R., & Chun, M. M. (2000). Organization of visual short-term memory. *J Exp Psychol Learn Mem Cogn, 26*(3), 683-702.

Kanwisher, N., McDermott, J., & Chun, M. M. (1997). The fusiform face area: a module in human extrastriate cortex specialized for face perception. *J Neurosci, 17*(11), 4302-4311.

Klaver, P., Smid, H. G., & Heinze, H. J. (1999). Representations in human visual short-term memory: an event-related brain potential study. *Neurosci Lett, 268*(2), 65-68.

Klemen, J., Buchel, C., Buhler, M., Menz, M. M., & Rose, M. (In press). Auditory Working Memory Load Impairs Visual Ventral Stream Processing: Toward a Unified Model of Attentional Load. *J Cogn Neurosci*.

Kumar, A., & Jiang, Y. (2005). Visual short-term memory for sequential arrays. *Mem Cognit, 33*(3), 488-498.

Lavie, N. (1995). Perceptual load as a necessary condition for selective attention. *J Exp Psychol Hum Percept Perform, 21*(3), 451-468.

Lavie, N., & De Fockert, J. (2005). The role of working memory in attentional capture. *Psychon Bull Rev, 12*(4), 669-674.

Lavie, N., Hirst, A., de Fockert, J. W., & Viding, E. (2004). Load theory of selective attention and cognitive control. *J Exp Psychol Gen, 133*(3), 339-354.

Lavie, N., & Tsal, Y. (1994). Perceptual load as a major determinant of the locus of selection in visual attention. *Percept Psychophys, 56*(2), 183-197.

Leung, H. C., Gore, J. C., & Goldman-Rakic, P. S. (2002). Sustained mnemonic response in the human middle frontal gyrus during on-line storage of spatial memoranda. *J Cogn Neurosci, 14*(4), 659-671.

Leung, H. C., Oh, H., Ferri, J., & Yi, Y. (2007). Load response functions in the human spatial working memory circuit during location memory updating. *Neuroimage, 35*(1), 368-377.

Leung, H. C., Seelig, D., & Gore, J. C. (2004). The effect of memory load on cortical activity in the spatial working memory circuit. *Cogn Affect Behav Neurosci, 4*(4), 553-563.

Leung, H. C., & Zhang, J. X. (2004). Interference resolution in spatial working memory. *Neuroimage, 23*(3), 1013-1019.

Linden, D. E., Bittner, R. A., Muckli, L., Waltz, J. A., Kriegeskorte, N., Goebel, R., Singer, W., & Munk, M. H. (2003). Cortical capacity constraints for visual working memory: dissociation of fMRI load effects in a fronto-parietal network. *Neuroimage, 20*(3), 1518-1530.

Logie, R. H., Zucco, G. M., & Baddeley, A. D. (1990). Interference with visual short-term memory. *Acta Psychol (Amst), 75*(1), 55-74.

Low, A., Rockstroh, B., Cohen, R., Hauk, O., Berg, P., & Maier, W. (1999). Determining working memory from ERP topography. *Brain Topogr, 12*(1), 39-47.

Luck, S. J., & Hillyard, S. A. (1995). The role of attention in feature detection and conjunction discrimination: an electrophysiological analysis. *Int J Neurosci, 80*(1-4), 281-297.

Luck, S. J., & Vogel, E. K. (1997). The capacity of visual working memory for features and conjunctions. *Nature, 390*(6657), 279-281.

Lueck, C. J., Zeki, S., Friston, K. J., Deiber, M. P., Cope, P., Cunningham, V. J., Lammertsma, A. A., Kennard, C., & Frackowiak, R. S. (1989). The colour centre in the cerebral cortex of man. *Nature, 340*(6232), 386-389.

Macoveanu, J., Klingberg, T., & Tegner, J. (2006). A biophysical model of multiple-item working memory: a computational and neuroimaging study. *Neuroscience, 141*(3), 1611-1618.

Makovski, T., Sussman, R., & Jiang, Y. V. (2008). Orienting attention in visual working memory reduces interference from memory probes. *J Exp Psychol Learn Mem Cogn, 34*(2), 369-380.

Malach, R., Reppas, J. B., Benson, R. R., Kwong, K. K., Jiang, H., Kennedy, W. A., Ledden, P. J., Brady, T. J., Rosen, B. R., & Tootell, R. B. (1995). Object-related activity revealed by functional magnetic resonance imaging in human occipital cortex. *Proc Natl Acad Sci U S A, 92*(18), 8135-8139.

Martin-Loeches, M., & Rubia, F. J. (1997). Encoding into working memory of spatial location, color, and shape: electrophysiological investigations. *Int J Neurosci, 91*(3-4), 277-294.

McCarthy, G., Puce, A., Constable, R. T., Krystal, J. H., Gore, J. C., & Goldman-Rakic, P. (1996). Activation of human prefrontal cortex during spatial and nonspatial working memory tasks measured by functional MRI. *Cereb Cortex, 6*(4), 600-

611.

McElree, B., & Dosher, B. A. (1989). Serial position and set size in short-term memory: The time course of recognition. *Journal of Experimental Psychology: General, 118*(4), 346-373.

McEvoy, L. K., Smith, M. E., & Gevins, A. (1998). Dynamic cortical networks of verbal and spatial working memory: effects of memory load and task practice. *Cereb Cortex, 8*(7), 563-574.

Mecklinger, A., & Pfeifer, E. (1996). Event-related potentials reveal topographical and temporal distinct neuronal activation patterns for spatial and object working memory. *Brain Res Cogn Brain Res, 4*(3), 211-224.

Miller, E. K., Erickson, C. A., & Desimone, R. (1996). Neural mechanisms of visual working memory in prefrontal cortex of the macaque. *J Neurosci, 16*(16), 5154-5167.

Mohr, H. M., Goebel, R., & Linden, D. E. (2006). Content- and task-specific dissociations of frontal activity during maintenance and manipulation in visual working memory. *J Neurosci, 26*(17), 4465-4471.

Mohr, H. M., & Linden, D. E. (2005). Separation of the systems for color and spatial manipulation in working memory revealed by a dual-task procedure. *J Cogn Neurosci, 17*(2), 355-366.

Morgan, H. M., Klein, C., Boehm, S. G., Shapiro, K. L., & Linden, D. E. (2008). Working Memory Load for Faces Modulates P300, N170, and N250r. *J Cogn Neurosci*, *20*(6), 989-1002.

Mottaghy, F. M., Gangitano, M., Sparing, R., Krause, B. J., & Pascual-Leone, A. (2002). Segregation of areas related to visual working memory in the prefrontal cortex revealed by rTMS. *Cereb Cortex, 12*(4), 369-375.

Munk, M. H., Linden, D. E., Muckli, L., Lanfermann, H., Zanella, F. E., Singer, W., & Goebel, R. (2002). Distributed cortical systems in visual short-term memory revealed by event-related functional magnetic resonance imaging. *Cereb Cortex, 12*(8), 866-876.

Ninokura, Y., Mushiake, H., & Tanji, J. (2003). Representation of the temporal order of visual objects in the primate lateral prefrontal cortex. *J Neurophysiol, 89*(5), 2868-2873.

Ninokura, Y., Mushiake, H., & Tanji, J. (2004). Integration of temporal order and object information in the monkey lateral prefrontal cortex. *J Neurophysiol, 91*(1), 555-560.

Oberauer, K., & Kliegl, R. (2001). Beyond resources: Formal models of complexity effects and age differences in working memory. *European Journal of Cognitive Psychology, 13*(1-2), 187-215.

Oberauer, K., & Kliegl, R. (2006). A formal model of capacity limits in working memory. *Journal of Memory and Language, 55*(4), 601-626.

Oberauer, K., & Lewandowsky, S. (2008). Forgetting in immediate serial recall: Decay, temporal distinctiveness, or interference? *Psychological Review, 115*(3), 544-576.

Oh, H., & Leung, H. C. (In press). Specific and Nonspecific Neural Activity during Selective Processing of Visual Representations in Working Memory. *J Cogn Neurosci*.

Olson, I. R., Page, K., Moore, K. S., Chatterjee, A., & Verfaellie, M. (2006). Working memory for conjunctions relies on the medial temporal lobe. *J Neurosci, 26*(17), 4596-4601.

Owen, A. M., Stern, C. E., Look, R. B., Tracey, I., Rosen, B. R., & Petrides, M. (1998). Functional organization of spatial and nonspatial working memory processing within the human lateral frontal cortex. *Proc Natl Acad Sci U S A, 95*(13), 7721-7726.

Peterson, L., & Peterson, M. J. (1959). Short-term retention of individual verbal items. *Journal of Experimental Psychology, 58*(3), 193-198.

Petit, L., Courtney, S. M., Ungerleider, L. G., & Haxby, J. V. (1998). Sustained activity in the medial wall during working memory delays. *J Neurosci, 18*(22), 9429-9437.

Picard, N., & Strick, P. L. (2001). Imaging the premotor areas. *Curr Opin Neurobiol, 11*(6), 663-672.

Postle, B. R., & D'Esposito, M. (1999). "What"-Then-Where" in visual working memory: an event-related fMRI study. *J Cogn Neurosci, 11*(6), 585-597.

Postle, B. R., Stern, C. E., Rosen, B. R., & Corkin, S. (2000). An fMRI investigation of cortical contributions to spatial and nonspatial visual working memory. *Neuroimage, 11*(5 Pt 1), 409-423.

Prime, S. L., Vesia, M., & Crawford, J. D. (2008). Transcranial magnetic stimulation over posterior parietal cortex disrupts transsaccadic memory of multiple objects. *J Neurosci, 28*(27), 6938-6949.

Rainer, G., Asaad, W. F., & Miller, E. K. (1998). Selective representation of relevant information by neurons in the primate prefrontal cortex. *Nature, 393*(6685), 577-579.

Ranganath, C., Cohen, M. X., Dam, C., & D'Esposito, M. (2004). Inferior temporal, prefrontal, and hippocampal contributions to visual working memory maintenance and associative memory retrieval. *J Neurosci, 24*(16), 3917-3925.

Ranganath, C., DeGutis, J., & D'Esposito, M. (2004). Category-specific modulation of inferior temporal activity during working memory encoding and maintenance. *Brain Res Cogn Brain Res, 20*(1), 37-45.

Rao, S. C., Rainer, G., & Miller, E. K. (1997). Integration of what and where in the primate prefrontal cortex. *Science, 276*(5313), 821-824.

Rose, M., Schmid, C., Winzen, A., Sommer, T., & Buchel, C. (2005). The functional and temporal characteristics of top-down modulation in visual selection. *Cereb Cortex, 15*(9), 1290-1298.

Rowe, J. B., & Passingham, R. E. (2001). Working memory for location and time: activity in prefrontal area 46 relates to selection rather than maintenance in memory. *Neuroimage, 14*(1 Pt 1), 77-86.

Ruchkin, D. S., Johnson, R., Jr., Grafman, J., Canoune, H., & Ritter, W. (1997). Multiple visuospatial working memory buffers: evidence from spatiotemporal patterns of brain activity. *Neuropsychologia, 35*(2), 195-209.

Rushworth, M. F., Nixon, P. D., Eacott, M. J., & Passingham, R. E. (1997). Ventral prefrontal cortex is not essential for working memory. *J Neurosci, 17*(12), 4829-4838.

Sakai, K., Rowe, J. B., & Passingham, R. E. (2002). Active maintenance in prefrontal area 46 creates distractor-resistant memory. *Nat Neurosci, 5*(5), 479-484.

Sakai, K., Watanabe, E., Onodera, Y., Uchida, I., Kato, H., Yamamoto, E., Koizumi, H., & Miyashita, Y. (1995). Functional mapping of the human colour centre with echo-planar magnetic resonance imaging. *Proc Biol Sci, 261*(1360), 89-98.

Sala, J. B., Rama, P., & Courtney, S. M. (2003). Functional topography of a distributed neural system for spatial and nonspatial information maintenance in working memory. *Neuropsychologia, 41*(3), 341-356.

Smith, E. E., & Jonides, J. (1997). Working memory: a view from neuroimaging. *Cognit Psychol, 33*(1), 5-42.

Smith, E. E., Jonides, J., & Koeppe, R. A. (1996). Dissociating verbal and spatial working memory using PET. *Cereb Cortex, 6*(1), 11-20.

Smith, E. E., Smith, E. E., Jonides, J., Koeppe, R. A., & Awh, E. (1995). Spatial versus object working memory: PET investigations. *Journal of Cognitive Neuroscience, 7*(3), 337.

Song, J. H., & Jiang, Y. (2006). Visual working memory for simple and complex features: an fMRI study. *Neuroimage, 30*(3), 963-972.

Todd, J. J., & Marois, R. (2004). Capacity limit of visual short-term memory in human posterior parietal cortex. *Nature, 428*(6984), 751-754.

Underwood, B. J. (1957). Interference and forgetting. *Psychol Rev, 64*(1), 49-60.

Ungerleider, L. G., & Mishkin, M. (1982). Two cortical visual systems. In D. J. Ingle & M. A. Goodale & R. J. W. Mansfielf (Eds.), *Analysis of visual behavior* (pp. 549-586). Cambridge: MIT press.

Vogel, E. K., & Machizawa, M. G. (2004). Neural activity predicts individual differences in visual working memory capacity. *Nature, 428*(6984), 748-751.

Vogel, E. K., Woodman, G. F., & Luck, S. J. (2001). Storage of features, conjunctions and objects in visual working memory. *J Exp Psychol Hum Percept Perform, 27*(1), 92-114.

Vogel, E. K., Woodman, G. F., & Luck, S. J. (2006). The time course of consolidation in visual working memory. *J Exp Psychol Hum Percept Perform, 32*(6), 1436-1451.

Vuontela, V., Rama, P., Raninen, A., Aronen, H. J., & Carlson, S. (1999). Selective interference reveals dissociation between memory for location and colour. *Neuroreport, 10*(11), 2235-2240.

Warden, M. R., & Miller, E. K. (2007). The representation of multiple objects in prefrontal neuronal delay activity. *Cereb Cortex, 17 Suppl 1*, i41-50.

Watter, S., Geffen, G. M., & Geffen, L. B. (2001). The n-back as a dual-task: P300 morphology under divided attention. *Psychophysiology, 38*(6), 998-1003.

Waugh, N. C., & Norman, D. A. (1965). Primary memory. *Psychological Review, 75*, 89-104.

Wheeler, M. E., & Treisman, A. M. (2002). Binding in short-term visual memory. *J Exp Psychol Gen, 131*(1), 48-64.

Xu, Y. (2002). Encoding color and shape from different parts of an object in visual short-term memory. *Percept Psychophys, 64*(8), 1260-1280.

Xu, Y., & Chun, M. M. (2006). Dissociable neural mechanisms supporting visual short-term memory for objects. *Nature, 440*(7080), 91-95.

Yakovlev, V., Bernacchia, A., Orlov, T., Hochstein, S., & Amit, D. (2005). Multi-item working memory--a behavioral study. *Cereb Cortex, 15*(5), 602-615.

Yoon, J. H., Curtis, C. E., & D'Esposito, M. (2006). Differential effects of distraction during working memory on delay-period activity in the prefrontal cortex and the visual association cortex. *Neuroimage, 29*(4), 1117-1126.

Zeki, S., Watson, J. D., Lueck, C. J., Friston, K. J., Kennard, C., & Frackowiak, R. S. (1991). A direct demonstration of functional specialization in human visual cortex. *J Neurosci, 11*(3), 641-649.

Zelinsky, G. J., & Loschky, L. C. (2005). Eye movements serialize memory for objects in scenes. *Percept Psychophys, 67*(4), 676-690.

Zoccolan, D., Cox, D. D., & DiCarlo, J. J. (2005). Multiple object response normalization in monkey inferotemporal cortex. *J Neurosci, 25*(36), 8150-8164.