

# Binding of verbal and spatial information in human working memory involves large-scale neural synchronization at theta frequency

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Whether neural synchronization is engaged in binding of verbal and spatial information in working memory remains unclear. The present study analyzed oscillatory power and phase synchronization of electroencephalograph (EEG) recorded from subjects performing a working memory task. Subjects were required to maintain both verbal (letters) and spatial (locations) information of visual stimuli while the verbal and spatial information were either bound or separate. We found that frontal theta power, and large-scale theta phase synchronization between bilateral frontal regions and between the left frontal and right temporal–parietal regions were greater for maintaining bound relative to separate information. However, the same effects were not observed in the gamma band. These results suggest that working memory binding involves large-scale neural synchronization at the theta band.

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## Introduction

Working memory allows the current task-related information to be temporarily stored and manipulated. The model of working memory proposed by Baddeley and Hitch (1974) includes an attention controller, the central executive and two subsidiary systems (i.e., the phonological loop and the visuospatial sketchpad) for holding verbal and visual information respectively. Recently, much attention has been paid to the brain mechanisms involved in the integration of different information in working memory, and the episodic buffer, a new component of working memory which emphasizes the integration of information from a number of sources is proposed (for review, see Baddeley, 2000).

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There were neuroimaging studies examining feature conjunction in working memory with the match-to-sample task (Shafritz et al., 2002; Simon-Thomas et al., 2003). Using functional magnetic resonance imaging (fMRI), Shafritz et al. (2002) showed that the parietal cortices were more involved in feature conjunction task than in single feature tasks (color or shape). The event-related potential (ERP) study of Simon-Thomas et al. (2003) found that the P300 at the retrieval period was stronger in the processing of combined features than in the processing of single features (form or location). This observation suggested that feature conjunction “upregulates frontal–parietal association networks” (Simon-Thomas et al., 2003). The EEG study of Busch and Herrmann (2003) varied the numbers of objects and features independently and found that object load and feature load influenced short-term memory task at different stages. Specifically, during the maintenance period, the induced 10 Hz oscillation was modulated by object load rather than feature load supporting the view that information storage in short-term memory is object-based rather than feature-based.

Moreover, two experiments (Prabhakaran et al., 2000; Campo et al., 2005) investigated the neural basis of binding verbal and spatial information in working memory. In a paradigm designed to compare the bound and separate condition, letters (letters in Prabhakaran et al. (2000) and words in Campo et al. (2005)) and locations were remembered either conjointly as they were presented together, or separately as the verbal information appeared in other locations. Using fMRI, Prabhakaran et al. (2000) showed that the frontal areas were involved in binding of verbal and spatial information in working memory during the maintenance period. Campo et al. (2005) analyzed sources of the evoked event-related field (ERF) in a magnetoencephalography (MEG) study. They found that in addition to the frontal areas, the temporal–parietal areas were involved in the binding process during the maintenance period as well. Importantly, the results of Campo et al. (2005) also showed that the binding-related activity took place in early latencies of the maintenance period, which provided unique temporal information to the understanding of the brain processes involved in working memory binding.

Taken together, previous neuroimaging studies have investigated the neural substrates of working memory binding, particularly where and when the binding process takes place. These findings suggest that working memory binding involves both frontal and temporal–parietal areas, and the bound and unbound information are processed at different stages.

Another important mechanism for binding is neural synchro-

Whether that particular letter had been in that particular parenthesis was not regarded. For both the bound and separate

spurious synchronization resulting from the volume conduction in some extent (Rodriguez et al., 1999).

*Sa, c e h d*

*Ge e a f TFP, g fca ce a,*

Power values in the bound and separate conditions were directly compared by paired  $t$ -test. The resulting  $P$  values were then subjected

to the random permutation test (Kaiser et al., 2004; Summerfield and Mangels, 2005) to correct for the type-I error during multiple comparisons (there were 32 electrodes for power comparisons). Corrections for TFP were based on TFP pixels. Subject-condition power values were swapped 1000 times. In each permutation the  $t$ -test repeated for each electrode and the maximum  $P$  value from all the electrodes was logged for each permutation. The TFP pixels whose values fell within the 95th percentile ( $P$  value  $\leq 0.05$ ) of the

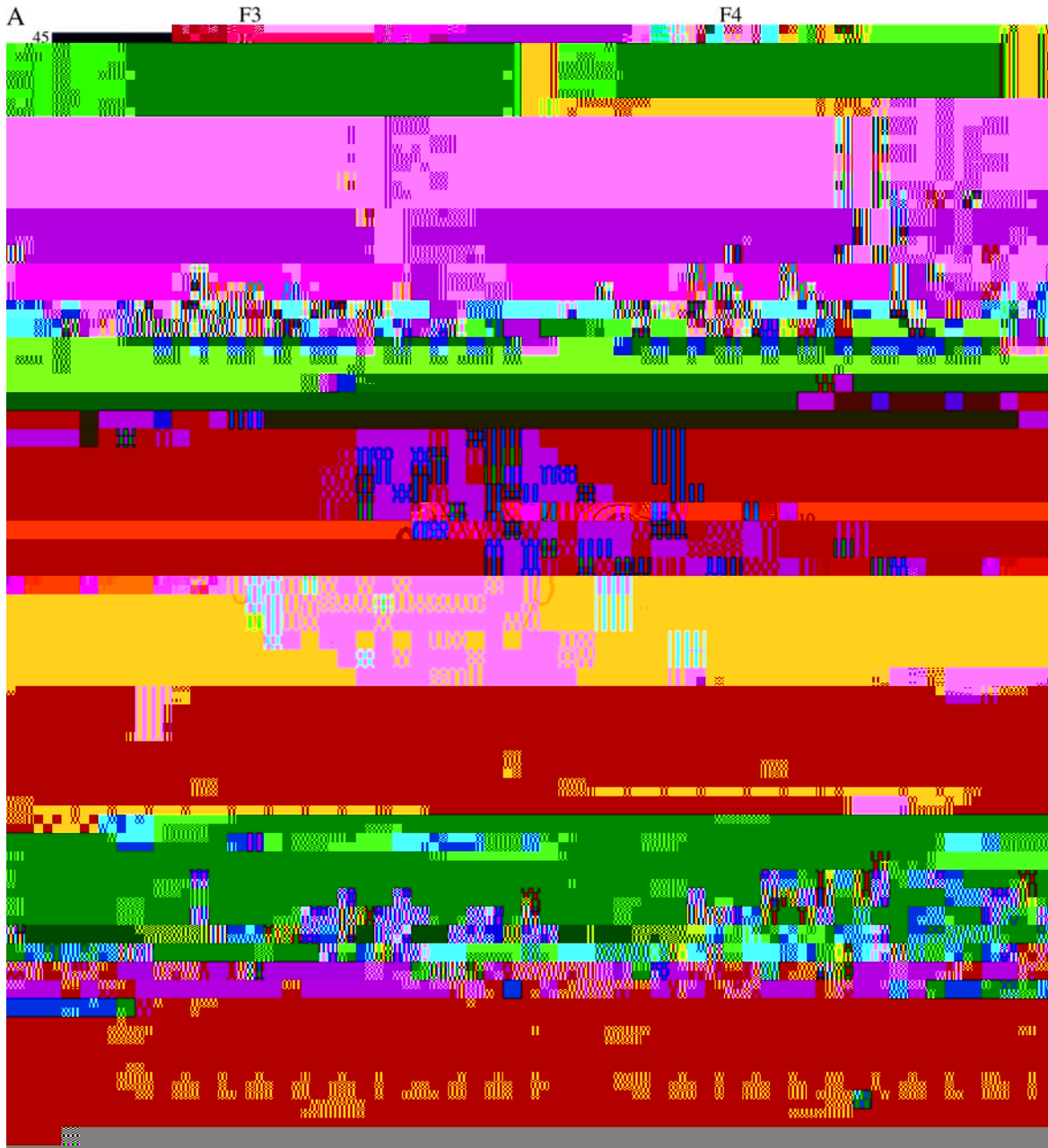
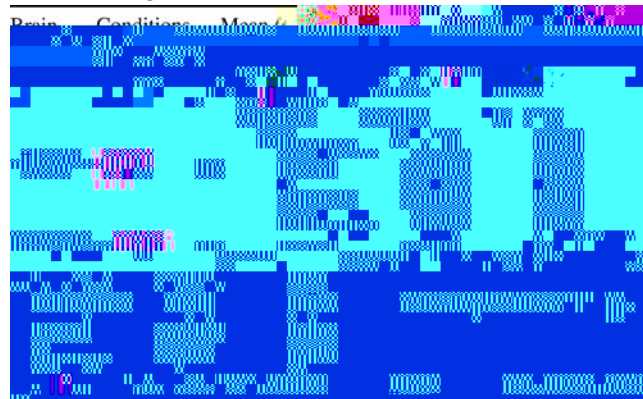


Fig. 2. Greater frontal theta power (about 6 Hz) in the bound than in the separate condition. (A) Time-frequency power (TFP) significance maps of two frontal electrodes (F3 and F4). Increased power in the bound than in the separate condition was observed at about 6 Hz during the time window of about 2.2–6.5 s. The color indicates the scale of  $P$  values ( $\leq 0.05$ ). The top part of the color bars indicates greater whereas the bottom part indicates lesser power in the bound relative to

Table 1  
The 6 Hz power comparison between the bound and separate conditions in the four brain regions



The paired  $t$ -tests were performed on the power differences with the  $P$  values less than 0.05 marked in red. LF: left frontal region; RF: right frontal region; LP: left temporal–parietal region; RP: right temporal–parietal region.

distribution of maximum shuffled values were deemed to be significant. In addition, because  $P$  values are always positive, we could thus not indicate whether the power was greater or less in the bound than in the separate condition, which is respectively indicated by the top and bottom parts of color bars in the significance map (see

Fig. 2A). The identified TFOI was then used for phase synchronization analyses.

Phase synchronization values in TFOI were firstly averaged (Rodriguez et al., 1999; Gross et al., 2004) and then directly compared by paired  $t$ -test between the bound and separate conditions. The random permutation test (Kaiser et al., 2004; Summerfield and Mangels, 2005) was also performed to correct for the type-I error during multiple comparisons (there were 66 electrode pairs for phase synchronization comparisons). Corrected  $P$  value  $\leq 0.05$  was set as the significance threshold.

**Result**

*Beha da a*

Subjects performed significantly ( $t = 2.82, P = 0.017$ ) better in the bound (Mean accuracy = 89.2%, MSE = 1.5%) than in the separate (Mean accuracy = 86%, MSE = 1.4%) condition. For the reaction times (RT), though the condition difference did not reach significance ( $t = -1.549, P = 0.165$ ), subjects did respond faster in the bound (Mean RT = 1232 ms, MSE = 42 ms) compared to the separate (Mean RT = 1299 ms, MSE = 74 ms) condition. These results were consistent with previous studies (Prabhakaran et al., 2000; Simon-Thomas et al., 2003; Campo et al., 2005), indicating that binding decreases the task difficulty.

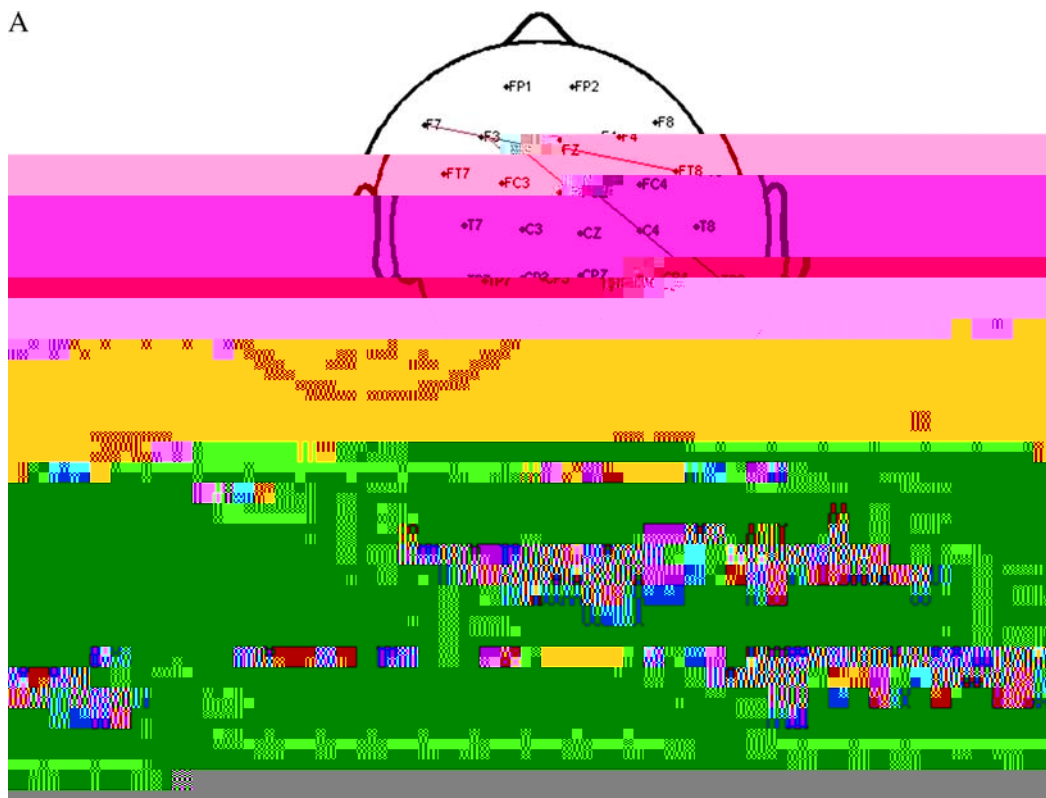


Fig. 3. Greater 6 Hz phase synchronization in the bound than in the separate condition. (A) Phase synchronization significance map for the 6 Hz frequency. Electrode pairs in which the 6 Hz phase synchronization was significantly ( $P \leq 0.05$ ) different between the bound and separate conditions are plotted on the scalp. Red and blue lines respectively indicate phase synchronization being greater and lesser in the bound than in the separate condition. Here no blue line was obtained. (B) The mean time courses of the 6 Hz phase synchronization of electrode pairs F7-FT8 and F3-TP8.

EEG data

Power spectral density

In the bilateral frontal regions, the power was significantly greater in the bound than in the separate condition at about 6 Hz and during the time interval of about 2.2–6.5 s (Fig. 2). This effect was not found in the gamma or other frequency bands. The time interval of 2.2–6.5 s and the frequency of 6 Hz were then taken as the TFOI and used for phase synchronization analyses.

Fig. 2 provided the power information about single electrode, and the power values of the averaged electrodes were also calculated. They may complement each other. For the 12 electrodes located in the four brain regions (as mentioned above), the power values in the TFOI were averaged for each brain region. The Mean, MSE of power in the bound and separate conditions and the power differences between the two conditions are listed in Table 1. The paired  $t$ -tests were performed on the power differences (Table 1), showing that over the bilateral frontal regions, the 6 Hz power was significantly greater in the bound than in the separate condition, which was consistent with Fig. 2.

Phase synchronization

Between bilateral frontal regions and between the left frontal and right temporal-parietal regions, the 6 Hz phase synchronization was significantly greater in the bound than in the separate condition (Fig. 3)<sup>3</sup>.

Same to the power analyses, the phase synchronization values of the averaged electrode pairs were also calculated. For the

The greater frontal theta power and the greater theta phase synchronization between bilateral frontal regions in the bound condition suggest the engagement of the frontal areas in the

verbal and spatial information were either bound or separate. We found that the frontal theta power and large-scale theta phase synchronization between bilateral frontal regions and between the left frontal and right temporal–parietal regions were greater for maintaining bound relative to separate information. Our results suggest that large-scale neural synchronization at the theta band is involved in working memory binding thus provides the neurophysiological evidence supporting the temporal binding hypothesis in working memory (Singer, 1999; von der Malsburg, 1999; Baddeley, 2000). However, the present results do not oppose to the classical binding theory (Barlow, 1972; Riesenhuber and Poggio, 1999). As Singer (1999) suggested, the temporal binding mechanism and the classical binding mechanism may complement rather than contradict each other in the binding processes.

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### **Appendi A**

One reviewer suggested that the number of cycles of wavelets (NCW)=10 used in the main text may be too large for the 40 Hz activity and this may be a possible account for the absence of



- temporal limitations of visual attention in humans. *Proc. Natl. Acad. Sci. U. S. A.* 101, 13050–13055.
- Haxby, J.V., Petit, L., Ungerleider, L.G., Courtney, S.M., 2000. Distinguishing the functional roles of multiple regions in distributed neural systems for visual working memory. *NeuroImage* 11, 380–391.
- Herrmann, C.S., Mecklinger, A., Pfeifer, E., 1999. Gamma responses and ERPs in a visual classification task. *Clin. Neurophysiol.* 110, 636–642.
- Howard, M.W., Rizzuto, D.S., Caplan, J.B., Madsen, J.R., Lisman, J., Aschenbrenner-Scheibe, R., Schulze-Bonhage, A., Kahana, M.J., 2003. *Cereb. Cortex* 13, 1369–1374.
- Jensen, O., Tesche, C.D., 2002. Frontal theta activity in humans increases with memory load in a working memory task. *Eur. J. Neurosci.* 15, 1395–1399.
- Jonides, J., Schumacher, E.H., Smith, E.E., Koeppe, R.A., Awh, E., Reuter-Lorenz, P.A., Marshuetz, C., Willis, C.R., 1998. The role of parietal cortex in verbal working memory. *J. Neurosci.* 18, 5026–5034.
- Kahana, M.J., Seelig, D., Madsen, J.R., 2001. Theta returns. *Curr. Opin. Neurobiol.* 11, 739–744.
- Kaiser, J., Buhler, M., Lutzenberger, W., 2004. Magnetoencephalographic gamma-band responses to illusory triangles in humans. *NeuroImage* 23, 551–560.
- Klimesch, W., Doppelmayr, M., Schwaiger, J., Auinger, P., Winkler, T., 1999. ‘Paradoxical’ alpha synchronization in a memory task. *Cogn. Brain Res.* 7, 493–501.
- Lachaux, J.P., Rodriguez, E., Martinerie, J., Varela, F.J., 1999. Measuring phase synchrony in brain signals. *Hum. Brain Mapp.* 8, 194–208.
- Luck, S.J., Vogel, E.K., 1997. The capacity of visual working memory for features and conjunctions. *Nature* 390, 279–281.
- Mizuhara, H., Wang, L.Q., Kobayashi, K., Yamaguchi, Y., 2004. A long-range cortical network emerging with theta oscillation in a mental task. *NeuroReport* 15, 1233–1238.

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