Hemispheric Asymmetry for Encoding Unrelated Word Pairs? A Functional Near-infrared Spectroscopy Study*

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Abstract **Objective** To explore the role of the prefrontal cortex in semantic encoding of unrelated word pairs by using functional near-infrared spectroscopy (fNIRS). **Method** Forty-eight subjects were presented unrelated pairs of Chinese words under both the nonsemantic and semantic encoding conditions. Under the nonsemantic condition, subjects judged whether the two words had similar orthographic structures; under the semantic condition, they generated a sentence involving the presented word pairs. The changes of regional blood volume associated with the cognitive tasks were measured by using fNIRS equipment which was a continuous optical imager. **Result** The regions that corresponded to the prefrontal regions showed greater activation under semantic than nonsemantic condition in both left and right hemispheres, although the extent of the activation was larger in the left than right prefrontal regions. This result was consistent with other neuroimaging studies on unrelated word pairs processing, but did not conform to the strict interpretations of the hemispheric encoding/retrieval asymmetry model (HERA). **Conclusion** This study suggests that material specificity is one of the important factors to influence hemispheric asymmetry in memory encoding. When associations between items are required, right prefrontal regions participate in the encoding processing as well. It also indicates that fNIRS imaging is a viable method of investigating higher level cognitive processing such as memory.

Key words functional near-infrared spectroscopy (fNIRS); prefrontal cortex; unrelated word pairs; hemispheric encoding/retrieval asymmetry model (HERA); memory

编码非相关词对是否具有半球对称性？一项近红外光学成像的研究. 杨炯炯, 曾少群, 骆清铭, 管林初, 匡培梓, 龚 辉, Lichty Wemara, Chance Britton. 航天医学与医学工程, 2005, 18(5): 318~323

摘要: **目的** 本研究采用近红外光学成像技术 (fNIRS), 探讨双侧前额叶在非相关词对的语义编码过程中的作用。**方法** 48名被试者分别在深、浅加工 2种实验条件下对非相关词对进行编码, 光学成像器即时记录在前额叶皮层, 波长为 760 nm和 850 nm的漫射光强变化, 以此推测相应脑组织的血容量变化。**结果** 与浅加工相比, 在深加工条件下, 双侧前额叶中与背外侧前额叶相对应区域的血容量变化都较为明显, 尤其是左侧前额叶。本研究结果并不完全支持 HERA模型, 但与其它相关的脑成像研究结果相似。**结论** 材料的特异性是影响记忆编码中半球一侧化的重要因素, 当需要对刺激间的联系进行加工时, 右侧前额叶也会参与记忆的编码过程。本研究还提示 fNIRS技术可用于记忆等脑高级认知功能的研究。

关键词: 功能近红外光学技术; 前额叶; 非相关词对; 记忆的编码与提取半球不对称性模型; 记忆
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Using functional neuroimaging techniques such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), many researchers have studied the role of the prefrontal cortex in episodic memory, which concerns memories for events or experiences[1, 2]. One of the memory models that has received considerable attention is the hemispheric encoding/retrieval asymmetry model (HERA) posited by Tulving *et al*[3]. It proposes that the left prefrontal cortex contributes more to encoding while the right prefrontal cortex contributes more to retrieval processes. This proposal has gained supports from many studies using verbal materials such as single words

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and related word pairs (e. g. animal—tiger). For example, Kapur *et al*[4] asked subjects to process visually presented words under either deep encoding condition (to categorize the noun as living or nonliving) or shallow condition (to judge whether the letter "a" was in the word). The PET results showed that the regional cerebral blood flow (rCBF) of the left prefrontal cortex increased significantly when the deep condition was compared with the shallow condition. No activation was found in the right prefrontal cortex. In another study, when subjects were asked to retrieve the studied words, the right prefrontal cortex was activated more than the left[5]. The acquisition of the related word pairs was also associated with activity in the left prefrontal cortex, whereas retrieval was associated with activity in the right prefrontal cortex[6].

However, there still remain some debates in recent years about the HERA model, especially concerning encoding process[7~9]. Encoding conditions involving nonverbal stimuli, such as unfamiliar faces and pictures, sometimes yielded bilateral or right-lateralized activations in the prefrontal cortex[1, 10~12]. Additional exceptions to the HERA model of left hemispheric dominance for encoding have been found in verbal studies demonstrating bilateral activation related to unrelated word pairs (e. g. candle—street). A PET study revealed increases in rCBF in bilateral frontal areas during encoding of word pairs[13]. Using fMRI, Mottaghy *et al*[14] showed that during encoding of unrelated word pairs activation was observed in bilateral frontal areas as well, with an augmentation on the left side. It is speculated that episodic encoding asymmetry is related to the nature of the material being encoded, and even left-lateralization for encoding of verbal material might be influenced by the type of verbal material used. The purpose of our study was to determine whether the right prefrontal cortex contributes to semantic encoding of unrelated word pairs, and whether there is difference between the activation of the left and right prefrontal cortex.

For our investigation, we used functional near-infrared spectroscopy (fNIRS), an optical imaging technique that can measure brain activation in vivo. Light with wavelengths of 760 nm and 850 nm have different absorption characteristics with respect to oxyhemoglobin (Oxy-Hb) and deoxyhemoglobin (Deoxy-Hb). The relative changes of Oxy-Hb and Deoxy-Hb can be detected and then applied to determine the blood volume (or the blood concentration) within the measured regions[15~18]. Studies have shown that fNIRS findings are consistent with the results of PET and fMRI[19, 20]. NIRS has been used to measure the cognition-related activation of the prefrontal cortex[21~24]. For example, Hoshi & Tamura[25] used fNIRS to examine the spatio-temporal differences of brain activation when subjects attempted to solve different mathematical problems. Blood oxygenation changes during language processing have also shown language-related responses in the prefrontal regions[26].

In the present study, we used the fNIRS imager to explore whether the encoding of unrelated word pairs would confirm the left-lateralized hemispheric asymmetry predicted by the HERA model, or confirm the bilateral findings in other studies about encoding of unrelated word pairs. Memory encoding was manipulated by providing a nonsemantic or semantic task. Regional blood volume changes in the prefrontal areas were measured during both tasks. By comparing the differences in blood volume changes between the left and right prefrontal areas, we expected to obtain the evidence concerning the role of prefrontal cortex in semantic encoding of unrelated word pairs.

Method

Subjects Forty-eight healthy, right-handed university students (age range 18~22, mean age 20.2, half male) participated in the experiment. They all had normal or corrected-to-normal vision, and none had a personal or family history of neurological or psychiatric illness.

Materials Fifty unrelated Chinese word pairs were compiled for the study, for example, rose-magnet. Each word in the pair, which had moderate frequency (mean 368 per million), was a compound composed of two Chinese characters. Each character was used only once in the experiment. Five pairs were used as the practice pairs. Another 5 pairs were used as filler pairs, three at the beginning of the list and two at the end. The remaining 40 word pairs were used as the study stimuli. They were divided into two sets, each having 20 pairs. Each subject was presented both lists, with the order of the lists and the tasks being counterbalanced.

Procedure The subjects were randomly divided into two groups according to whether their left or right prefrontal regions was measured (LPF, RPF). Each subject was randomly assigned to one of two task orders (nonsemantic followed by semantic, or semantic followed by nonsemantic). For the nonsemantic task, subjects were asked to judge whether the two words had similar orthographic structures. In the semantic condition, the subjects were asked to generate a meaningful sentence using the two words. A fixation point "+" was first presented at the center of the screen for 500 ms. Each word pair was then presented for 5 s and then disappeared, replaced with the next fixation point. Following the presentation of each list, the subjects were asked to relax completely, repeating "I'm now resting" silently and continuously. When the second task and rest sequence finished, the subjects performed an incidental recognition test to judge the presented word pairs were old/recombined ones.

The sequence of the experiment for each subject was rest 1 (30 s) –semantic or nonsemantic encoding (150 s) – rest 2 (60 s) –nonsemantic or semantic encoding (150 s) – rest 3 (180 s) –recognition test. The imager was used during the encoding session, but not during the recognition test.

Data acquisition The fNIRS equipment was a continuous wave light imager having nine sources and four probes of two wavelengths of 760 nm and 850 nm[16, 21]. The total size of the imager is 9 cm × 4 cm. As shown in figure 1, there were 16 detection channels based upon all possible combinations of the source/detector from which adequate signals were obtained. In each channel, the distance between the source and the detector was 2.5 cm. The imager was either placed on subjects' left or right forehead. In measuring the activation of left prefrontal cortex, the right edge of the imager reached the middle of the forehead, and the upper edge was close to the hairline. The left edge reached to EEG electrode positions F7 according to the International 10/20 system. From these scalp positions, fNIRS signals were obtained on the left anterior and dorsal part of the prefrontal brain areas. To measure the right prefrontal cortex, the detection areas were symmetrical to the left.

Data analysis The light intensity change were transformed to optical density change ($\triangle O.D.$) for each of the wavelengths: $\triangle O.D. = \lg(I_0/I_{test}) - \lg(I_0/I_{rest}) = \lg(I_{rest}) - \lg(I_{test})$ (where I_0 represents the incident light intensity, I_{rest} and I_{test} represent the light intensity during rest and task performance). The blood volume (BV) change was calculated by the algebraic expression: $\triangle O.D._{bv} = \triangle O.D._{850} + k\triangle O.D._{760}$. (Constant k is the modification factor for reducing the crosstalk between the changes of blood volume and oxygenation.)[21]. In order to better analyze the data, the 16 channels were divided into 4 regions in each hemisphere (see figure 1 for detail).

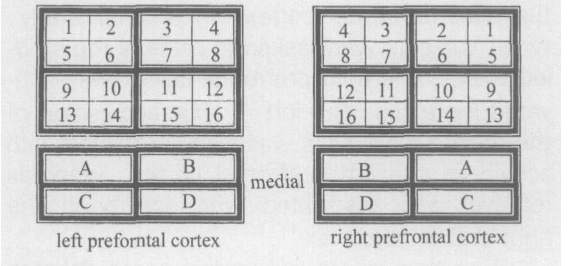

Fig 1 Detection regions in bilateral prefrontal areas

The imager was either placed on the left or right forehead. In order to analyze the data, the 16 channels were divided into 4 regions in both left and right prefrontal areas. For example, region A includes channel 1, 2, 5 and 6. The regions on the left and right were symmetrical, thus regions A and C were more lateral, and regions B and D were more medial.

To obtain the BV change related to encoding levels, the baseline BV obtained in the rest period immediately preceding the task was subtracted from the task BV. The BV difference between tasks was obtained by subtracting the BV of the nonsemantic task from that of the semantic task: $BV_{Difference} = (BV_{Semantic} - BV_{PreceedingRest}) - (BV_{Nonsemantic} - BV_{PreceedingRest})$. We took the upper point of $\triangle O.D.$ as 0.3 to eliminate possible artifacts.

Result

Behavioral performance For the recognition task, we calculated the proportion of pairs correctly recognized (hit-rate) and the recombined pairs incorrectly attributed to the study list (false-alarm rate) (see table 1). A 2 (hemisphere) x 2 (encoding process: nonsemantic, semantic) analysis of variance (ANOVA) was performed. The method of inducing encoding processing differences was successful as shown by the significantly superior recall of semantically encoded words, with mean hit-rate being 0.38 for the nonsemantic task and 0.91 for the semantic tasks, $F(1, 46) = 36.78$, $P < 0.001$. The main effect for hemisphere and the interaction were not significant.

Table 1 Recognition scores of the hit-rate, false-alarm rate, d' and β in nonsemantic and semantic tasks ($\bar{x} \pm s$)

hemisphere	type of encoding	hit-rate	false-alarm rate	d'	β
left	nonsemantic	0.39±0.13	0.56±0.34	0.22±0.19	0.99±0.16
	semantic	0.92±0.12	0.30±0.19	3.61±1.38	0.43±0.59
right	nonsemantic	0.36±0.14	0.60±0.13	0.18±0.09	0.87±0.23
	semantic	0.89±0.14	0.31±0.28	3.43±1.10	0.56±0.25

$P > 0.05$. False-alarm rate, d' and β analyses yielded similar results.

fNIRS results While subjects encoded the word pairs, the blood volume increased in the prefrontal cortex under both the nonsemantic and semantic conditions relative to the baseline. Furthermore, the blood volume change was greater under the semantic than under nonsemantic condition. The fNIRS image of the blood volume change of all 48 subjects was shown in figure 2. In the nonsemantic and semantic tasks, the most activated region was region C bilaterally, but the extent was larger in the semantic task. When the two tasks were compared, both left and right prefrontal cortices showed the activation, especially region C.

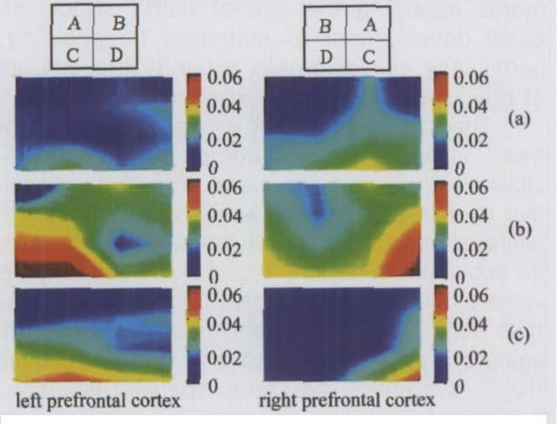

Fig. 2 Images of the blood volume difference in bilateral prefrontal regions between different task conditions

a. blood volume difference between uonsemantic and rest condition; b. blood volume difference between semantic and rest condition; c. blood volume difference between semantic and nousemantic condition

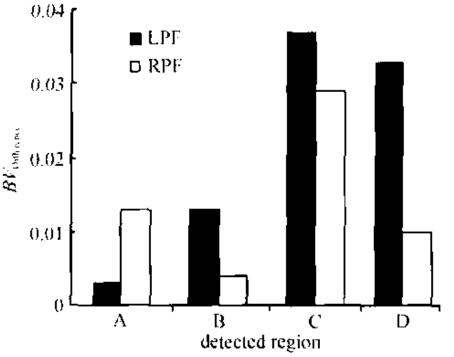

Fig 3 Blood volume difference between semantic and nonsemantic task in detected regions in both hemispheres

To determine the effect of encoding task, the $BV_{Difference}$ was analyzed by a 2 (hemisphere) x 4 (region A, B, C and D) ANOVA, with hemisphere as a between-subject variable and region as a within-subject variable (figure 3). The main effect of hemisphere was not significant, $F(1, 46) = 0.60$, $P = 0.44$. The main effect of region attained significance, $F(3, 138) = 6.76$, $P < 0.0001$, with post hoc tests revealing (A = B) < (C = D), suggesting the greatest activity was in the region that corresponds to the dorsolateral prefrontal cortex when hemispheric activity was combined. The interaction between hemisphere and region showed a trend, $F(3, 138) = 2.26$, $P = 0.08$. In the left prefrontal cortex, $BV_{Difference}$ in regions C and D were larger than in other two regions, $P < 0.05$, but regions C and D were not significantly different, $F(1, 23) = 0.15$, $P = 0.7$. In contrast, in the right prefrontal cortex, only the $BV_{Difference}$ in region C was significantly larger than other regions, $P < 0.05$. The $BV_{Difference}$ in region D showed significant difference ($P < 0.05$) between hemispheres, but $BV_{Difference}$ in region C was not significant, suggesting bilateral prefrontal regions play the important role in semantic encoding processing.

Discussion

In this study, we used fNIRS imaging technique to investigate the role of the prefrontal cortex in semantic encoding compared with nonsemantic encoding. The main findings were that blood volume increased bilaterally in the dorsolateral prefrontal cortex, with a more extensive blood volume increase in the left hemisphere (regions C and D) than in the right hemisphere (limited to region C).

For brain imaging investigations about encoding verbal material, many of the tasks have based on the effectiveness of semantic encoding for subsequent memory retrieval[27].

When the material is processed semantically (i.e. for meaning), memory on an unexpected (incidental) test is generally equivalent to memory on an expected (intentional) memory test[1], whereas memory for material processed nonsemantically is considerably lower. The recognition results of our data showed that the recall in the nonsemantic condition was very low and the recall in the semantic condition was about 2.5 times as great. Our imaging results supported the common PET and fMRI findings of activation of the dorsolateral prefrontal cortex when the semantic condition was compared with the nonsemantic condition[1, 10].

Regarding the HERA model prediction of left lateralization for verbal encoding, the bilateral activation we found did not conform to the strict interpretations of the HERA model[3, 7], which suggested that left prefrontal cortical regions are involved in encoding information, but right prefrontal areas are not, at least insofar as verbal information is concerned. Our data did not support the encoding aspect of the HERA model, because the right prefrontal area also showed activations in semantic encoding processing. On the other hand, our findings were consistent with previous studies using other functional brain imaging techniques such as PET and fMRI, which showed bilateral prefrontal cortical areas activated when subjects were encoding unrelated word pairs[13~14]. In addition, the presence of bilateral activation during semantic encoding of verbal material is not uncommon e.g., [28 (Fig 1), 29 (p 5875), 30 (Fig 1)]. In the studies that revealed bilateral activation, the activation of the left hemisphere predominated, as was also true of our study.

The experimental design of our study was similar to that of Kapur *et al*[4] and other studies. However, the stimuli we used, unrelated word pairs, were different from theirs and may account for the bilateral prefrontal activation. As mentioned in introduction, other neuroimaging studies using unrelated word pairs, rather the single words typically presented, revealed bilateral prefrontal activations as well[13, 14]. During encoding processing, subjects must not only process words individually, but also integrate them by processing the relations between them. The left hemisphere may be more adept at representing local information and the right hemisphere is better with global information. Consequently, association between unrelated words may require the right prefrontal cortex or the interaction of both hemispheres. In contrast, the association process is not needed in encoding single words, thus laterality is more pronounced. Our results supported the view that the HERA model is influenced by material specificity[11, 12], e.g., when the task requires forming associations between items.

The fact that we have bilateral activation; whereas, it is not found in many previous studies may also relate to statistical thresholding methods used to define regions of activation in PET and fMRI studies. As Fletcher and Henson noted, “the failure of a given region to survive such thresholding does not mean that we can exclude it from consideration.” [2, p 874]. Because fNIRS imaging is a fairly new technology, thresholding techniques have not yet been developed, thus our finding of bilateral activation may be a matter of survival scans thresholding. On the other hand, even if thresholding techniques had been applied in our study, we would have found bilateral activation of the dorsolateral prefrontal cortex, for the blood volume changes in the left and right C regions were high and essentially equivalent. Future developments regarding the use of fNIRS should include development of statistical thresholding, particularly as equipment expands the amount of brain area that can be investigated.

The spatial resolution of the extant equipment is certainly not comparable to fMRI. However, our results were sufficiently sensitive to delineate greater activation of regions C bilaterally and D in the left hemisphere, and little activation in regions A and B. These findings were similar to those of fMRI and PET studies; thus suggesting the sensitivity of the fNIRS imaging equipment we used was good. Because fNIRS systems have poor spatial resolution, fine-grained localization could be improved by having MRI scans for each subject in the future.

Clearly, our findings support the viability of fNIRS for evaluating brain activation during higher level cognitive processing. Some advantages of fNIRS include portability, affordability, and ease of use[15, 18]. These in conjunction with the fact that it can be used repeatedly on the same subjects make it an useful tool for evaluating brain activation changes related to a variety of tasks, particularly those related to learning and memory over time. An additional asset of fNIRS suggested by Villringer and Chance[17] is that the biochemical specificity concerning oxygenated and deoxygenated hemoglobin means fNIRS can be employed to validate the presumed basis of the fMRI signal.

In sum, using NIRS we found bilateral activations in the prefrontal regions with weaker activation in the right hemisphere when compared the semantic with nonsemantic condition. It suggests that associational requirements influence hemispheric asymmetry of the prefrontal regions in memory encoding processing.

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