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Intrinsically organized network for word processing during the resting state

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ABSTRACT

Neural mechanisms underlying word processing have been extensively studied. It has been revealed that when individuals are engaged in active word processing, a complex network of cortical regions is activated. However, it is entirely unknown whether the word-processing regions are intrinsically organized without any explicit processing tasks during the resting state. The present study investigated the intrinsic functional connectivity between word-processing regions during the resting state with the use of fMRI methodology. The low-frequency fluctuations were observed between the left middle fusiform gyrus and a number of cortical regions. They included the left angular gyrus, left supramarginal gyrus, bilateral pars opercularis, and left pars triangularis of the inferior frontal gyrus, which have been implicated in phonological and semantic processing. Additionally, the activations were also observed in the bilateral superior parietal lobule and dorsal lateral prefrontal cortex, which have been suggested to provide top-down monitoring on the visual–spatial processing of words. The findings of our study indicate an intrinsically organized network during the resting state that likely prepares the visual system to anticipate the highly probable word input for ready and effective processing.

Reading is an essential part of our everyday life in a modern literary society, of which word processing plays an important role. In the last several decades, there has been extensive research on the neural mechanisms underlying word processing. Based on these findings, a dual route model has been proposed, which includes first a common visual neural pathway for processing the word form, and then two parallel phonological and lexico-semantic routes. For the visual processing of words, Cohen et al. [3] propose the left middle fusiform gyrus to be specifically responsible for the visual form processing of words (i.e., the visual word form area, VWFA, but see [18]). Beyond the visual processing route, the left superior temporal gyrus, left supramarginal gyrus, and left inferior frontal gyrus (pars operculars) are suggested to belong to the phonological route to subserve the phonological decoding of words [2]. Meanwhile, the left inferior temporal gyrus, left angular gyrus, and left inferior frontal gyrus (pars triangularis) are thought to be part of the lexico-semantic route for the semantic retrieval of words [1]. Additionally, the superior parietal lobule and intraparietal sulcus have been suggested to be involved in visual attention modulation during word processing [9].

A similar set of neural pathways has been identified by studies examining Chinese character-processing. Consistent with the VWFA identified with alphabetic scripts, Liu et al. [14] identified Chinese character-preferential regions in the ventral occipitotemporal cortex. The anterior (BA 45) and posterior (BA 44) inferior frontal gyri are found to respond to both Chinese characters and alphabetic words [2,13]. Additionally, some regions are uniquely recruited in Chinese character processing for their special square configurations (e.g., the left middle frontal gyrus [21]).

In addition to the investigation of neural regions involved in active word processing, researchers employ various functional connectivity methods to explore the functional and effective connectivity among these regions (structural equation modelling [11] and dynamic causal model [2]). These analyses have revealed active interactions between the specific word-processing regions (e.g., [7]) and provided new insights into the neural organization of the word-processing network.

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However, these studies have examined only the functional or effective connectivity between the word-processing regions when individuals are actively engaged in a particular word-processing task. It is unclear whether the word-processing regions are intrinsically organized during the resting state without any explicit task demand. In recent years, resting state functional connectivity MRI analysis (rs-fcMRI) has been extensively employed to examine the intrinsically organized functional connectivity patterns within or between distinct subsystems of the brain [22]. Recently, Zhang et al. [23] identified strong functional connectivity between face preferentially responsive regions during the resting state, namely the bilateral posterior fusiform gyrus, inferior occipital gyrus, and superior temporal sulcus. They suggested that "the existence of such network may reflect the fact that faces are not only the visual stimuli that we tend to have the highest processing expertise [24] but also the most common visual stimuli we tend to encounter in our everyday social life. Thus, this intrinsically organized face resting state network may prepare the visual system to anticipate to process faces, the most socially significant category of visual stimuli" (page 5).

Words are in many ways similar to faces. In a modern society, we encounter words frequently and extensively on a daily basis. We see words in books, magazines, newspapers as well as traffic signs and billboards. Further, most literate adults are expert at processing words. Thus, similar to face processing, even when individuals are not encountering any words, the visual system may also be prepared to anticipate a highly probable word input. If it is the case, one should expect an intrinsically organized word-processing network to be present even without explicit word-processing tasks. To the best of our knowledge, no study has directly tested this intriguing hypothesis. It should be noted, however, that Hampson et al. [6] examined the resting state functional connectivities of language-processing cortexes. Their analysis was only limited to Broca's areas, Wernicke's areas and premotor regions known to be involved in speech processing; they did not explore the functional connectivities of these areas to the early perceptual areas involved in the decoding of linguistic input generally and word input in particular. The aim of our study was thus to bridge this gap in the literature by investigating the intrinsic functional connectivity between the word-processing regions using the rs-fcMRI analysis.

Twenty-four right-handed Chinese undergraduates (mean age: 23 years, SD: 2.5 years, 8 females) with normal vision participated in this study. All subjects gave their written informed consent. The study was approved by the Human Research Protection Program of Tiantan Hospital, Beijing, PR China.

The experiment was divided into three phases. In the first phase, a 310-s resting session was scanned. Participants, unaware of the exact experimental design, were instructed to lie with their eyes closed, thinking of nothing in particular. In the second phase, a 240-s visual discrimination task was performed. At the beginning, a 6-s scanning of fixation was shown to allow for stabilization of magnetization, and another 10-s scanning of fixation was included at the end for the delay of hemodynamic response. The session included six 24-s blocks interleaved with five 16-s fixation epochs in which cross hair was presented (Fig. 1). Each block included six trials. The timing procedure in each trial was 500-ms of fixation, 500-ms of null, 500-ms of the first stimulus, 1000-ms of fixation, 500-ms of the second stimulus and 1000-ms of fixation. During the last fixation, participants judged whether the two stimuli were identical. Equal number of the same and different trails was included. The third phase was a localizing session in which the localizer consists of a Chinese character localizer task and a face localizer task (Fig. 1).

MRI scans were performed in a 3 T (Siemens Trio a Tim, German) scanner. A T2-weighted gradient-echo planar imaging sequence was used for fMRI scans, with the slice thickness = 4 mm, in-plane resolution = 3.75 mm × 3.75 mm, and repetition time/echo time = 2000 ms/30 ms. For each participant, high-resolution (voxel size: 1 mm × 1 mm × 1 mm, matrix size: 256 × 256 × 256) anatomical images were acquired using a T1-weighted, three-dimensional gradient-echo imaging sequence.

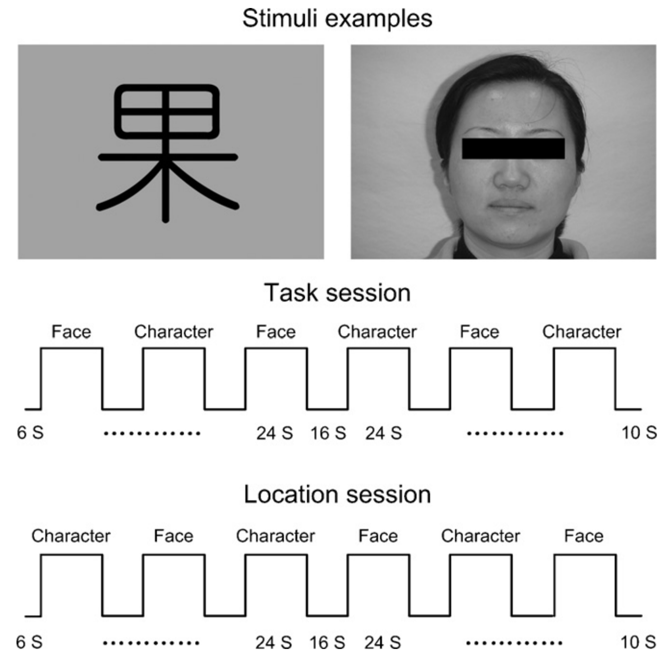

Fig. 1. Sample stimuli and the experiment design (eye region was shown during the experimental sessions but masked here for protection of privacy).

Before processing, the first three scans of each session were discarded. Data were analyzed using SPM5 (http://www.fil.ion.ucl.ac.uk/spm). Preprocess included slice timing, realignment, normalization to the standard EPI (MNI) template, and smoothness with a Gaussian kernel of 6-mm FWHM. For the resting and task sessions, global proportional scaling was performed respectively to yield a whole brain intensity value of 1000. Then, the data were temporally band-pass filtered (0.01 Hz < f < 0.08 Hz) using Resting-State fMRI Data Analysis Toolkit (http://www.restfmri.net).

For the localizer session, data were high-pass filtered to eliminate the low-frequency components (cut-off value of 128 s). A general linear model including two condition regressors (characters and faces) and six parameters for head motion was constructed for each participant. The condition regressor was created by convolving a canonical hemodynamic response function with a delta function corresponding to the onset time series of each stimulus category.

The seeding region of Chinese characters and faces were defined by the contrast of characters vs. faces and the reverse, with a statistical threshold $p < 0.0001$. The reason to contrast Chinese characters with faces was that Chinese characters and faces often activated similar regions in the ventral occipitotemporal cortex of Chinese participants. These contrasts thus allowed for identifying word-processing specific brain regions.

For the resting and task sessions, the time series averaged over the character-preferential region and face-preferential region, three null regressors of signals averaged over the whole brain (global signal), ventricles, and a region in deep cerebral white matter (picked by a sphere of 6-mm radius, centered at (26, −20, 30)), as well as six parameters for head motion were used as regressors to construct general linear model for each participant [22]. The functional connectivity mappings between the character-preferential region and all the other whole brain voxels were obtained using random-effect analysis across all subjects. The regions exceeding