Load Dependency of Correlation between Intrinsic Brain Activity and Brain Activation Induced by Working Memory Task

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Introduction

The intrinsic resting-state brain activity has been shown to be able to predict task induced brain activation [1-3]. However, a number of inconsistencies exist in these previous studies. Thus, it is critical to systematically investigate the relationship between resting-state activity and task induced activation. Furthermore, it is unknown whether the rest-task relationship would be parametrically modulated by task load. N-back cognitive tasks [4-6] have been extensively used to assess working memory (WM) capacity. Parametric manipulation of the task provides an opportunity to examine the dependency of the rest-task relationship on task load. Here, we acquired resting-state and parametric N-back [1, 2 and 3 back (1b, 2b, 3b)] WM task fMRI data on forty-one subjects and used a whole-brain voxel-wise regression approach to examine whether: 1) resting-state activity could predict task activation; and 2) the rest-task relationship would be dependent on task difficulty load.

Methods

Experimental design: Forty healthy subjects (27.1 ± 8.0 years old, 21 females) underwent a resting-state fMRI scan (8 minutes) during which they were asked to relax with their eyes closed, followed by a block-design N-back verbal WM task. The task was presented as a block paradigm with four conditions: three active WM tasks [1b, 2b, 3b] and a low level vigilance task [0 back (0b)].

Data acquisition: fMRI data were acquired with a gradient-echo echo-planar imaging (GE-EPI) sequence on a 3T Siemens MR scanner. The parameters for GE-EPI sequence were as follows: TR/TE = 2000/27 ms, FA=77°, slice thickness = 4mm without gap, 33 slices, FOV = 220×220 mm^2 with in-plane resolution = 3.44×3.44 mm^2.

Data analyses: All data analyses were conducted with AFNI [7], FSL [8], and MATLAB. Preprocessing steps for both resting-state and WM task data included slice timing and head motion correction, linear trend removal, and spatial smoothing with a 6-mm Gaussian kernel. For resting-state activity, we calculated voxel-wise fractional amplitude of low-frequency fluctuation (fALFF, [9]) for each subject. For the WM task data, general linear models (GLM) were constructed to obtain the task activation maps for the 1b, 2b and 3b conditions compared to the 0b condition. Finally, the fALFF and task activation maps were registered to standard TT space. To test whether fALFF could predict task activation, we conducted whole-brain voxel-wise correlation analyses at each WM level. To test whether the relationship between fALFF and task activation was dependent on the task loads, the same voxel-wise correlation analyses were conducted between fALFF and task activation differences ([A-B] contrast), i.e., [2b-1b], [3b-1b] and [3b-2b] contrasts, separately, to examine load dependency effect.

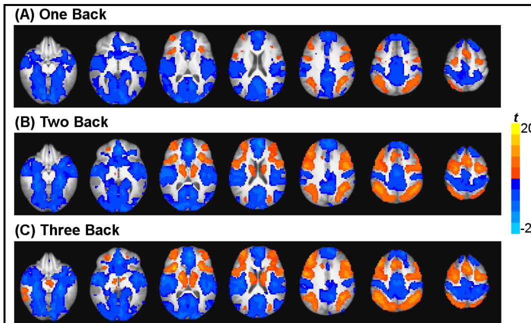

Fig. 1. N-back working memory task activation and deactivation under (A) 1b, (B) 2b and (C) 3b compared to vigilance baseline condition zero back.

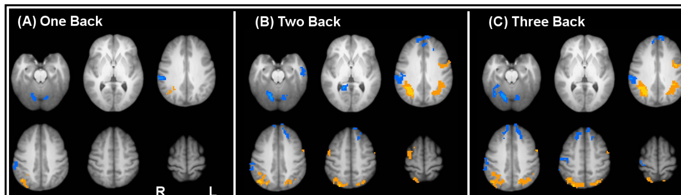

Fig. 2. Relationship between fALFF and task activation. Pearson correlation maps between fALFF and task activation under (A) 1b, (B) 2b and (C) 3b conditions.

Results

Rest-task relationship: In general, resting-state activity predicted task activation under all three WM task loads, though to a lesser extent under 1b (Fig. 2). The regions that showed significant rest-task relationship largely overlapped with task activated [IPL, superior parietal lobule (SPL), and middle frontal gyrus (MFG)] and deactivated regions [PCC, superior frontal gyrus (SFG)] (Fig. 1).

Load dependency effect of rest-task relationship: The rest-task relationship appears to be dependent on the WM task load, where the higher the task load, the better the resting metric predicted task activation. The greatest prediction power is generally seen when considering the differences between [2b-1b] and [3b-1b] (Fig. 3). The ability of rest to predict task activation in a load-dependent fashion is similar to the well-known effect of WM load increasing task-induced activation (Panels E and F).

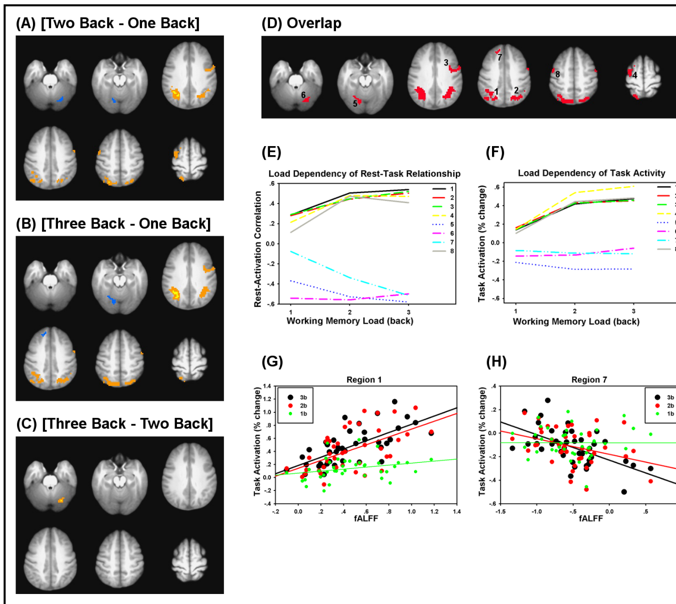

Fig. 3. Load dependency effect of the relationship between fALFF and task activity. Pearson correlation maps between fALFF and [2b - 1b] contrast (A), [3b - 1b] contrast (B) and [3b - 2b] contrast (C). (D) The overlap of regions that showed load dependency effect of fALFF-task relationship. (E) The average CC value in each region on panel (D) between fALFF and task activation under 1b, 2b and 3b. (F) The average task activation (% change) in each region on panel (D) under 1b, 2b and 3b. Scatter plots demonstrate the relationship between fALFF and task activation under 1b (green dots and line), 2b (red dots and line) and 3b (black dots and line) at region 1 on panel (D) (right IPL/SPL/PCU/SMG/AG) (G) and region 7 on panel (D) (right SFG) (H).

Summary and Discussion

In the current study, we demonstrated that spontaneous BOLD fluctuations robustly predicted subsequent WM task evoked activation at the IPL/SPL and MFG and predicted deactivation at the SFG. Our findings support the notion that intrinsic brain activity is related to the capacity and efficacy of particular brain circuits to perform a task [10, 11]. We further observed that the rest-task relationship depended on WM task load, i.e. there was a stronger rest-task relationship at the two higher WM task loads. The higher cognitive demands elicited larger average activations as well as wider dynamic range of the activations across subjects, which may help explain the stronger rest-task correlations at the higher WM task loads. Given the strong inter-subject correlation between resting-state activity and task activation, intrinsic resting-state activity would be useful for predicting the efficacy of brain function and even the severity of functional alterations in patients. In addition, resting-state activity might be used as a “normalizer” to reduce variations across subjects in task activation, thus increasing statistical power.

References

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