Improving Power of Permutation Test Using Unbiased Maximal Null Distribution for fMRI Data Analysis

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INTRODUCTION

Non-parametric statistical methods, such as permutation, are flexible tools to analyze data when the population distribution is not known. With minimal assumptions and better statistical power compared to the parametric tests, permutation tests have been applied to neuroimaging data of different imaging modalities, such as PET[1,2] and fMRI[3]. To perform permutation tests on neuroimaging data, an empirical maximal null distribution has to be found that is free from any activated voxels. The distribution is used to determine the threshold to define active voxels for a given probability level. An iterative procedure is used to determine the distribution by computing the null distribution. The distribution has to be recomputed when a possible activated voxel is found within the current distributions[4]. Besides the high computational costs associated with this approach, there is no guarantee that all activated voxels are excluded when constructing the maximal null distribution, which may reduce the statistical power. In this study we propose a novel way to construct the maximal null distribution to improve the power of the permutation test while reducing the computational cost at the same time.

METHOD

The general permutation test procedure is following: (1) Select a voxel-wise test statistic which measures the differences between conditions. (2) Compute the test statistic for the original condition labeling. (3) For each resampling, randomly rearrange the condition labels and compute the test statistic for the permuted data and add to the null distribution. (4) Repeat step 3 until a predefined number of resamplings has been performed. (5) Compare the null distribution of the test statistic to the original data. (6) Accept or reject the hypothesis based on the proportion of permuted test statistics equal to or greater than the original. To apply permutation tests on the neuroimaging data, a maximal statistic is used to construct the null distribution to perform the omnibus hypothesis test to avoid the multiple comparisons problem at the voxel level. In order to reduce the bias caused by including the active voxels, the maximal null distribution is usually constructed iteratively by checking whether there is any active voxel, which is in the extreme portion of the current distribution defined by a given probability level. If there are some active voxels, the null distribution will be reconstructed by removing these voxels. This reconstruction process is repeated until there is no voxel is defined as active under the newly constructed distribution. The maximal null distribution is then used to determine the threshold of the test statistic for a given p value. A new approach is proposed to ensure that there is no active voxel being used to construct the maximal null distribution. This can be done by defining a "dummy" active condition using the data from control condition to perform the steps (3) and (4) of the above procedure. The constructed maximal null distribution is then compared to the test statistic of the original data obtained in step (2).

RESULTS

To evaluate the performance of this new approach, a set of simulated data were created in a manner we have used in our previous simulation studies[5]. The data were created based on T2* weighted Echo-Planar Images (EPI) obtained from a single subject scanned with a GE 1.5T scanner. The dataset consisted of 5 axial slices (64x64 mm) of 320 scans; voxel size = 3.8x3.8x5.0mm. The baseline activities of the simulated datasets were generated with a first-order autoregressive plus a white-noise model. To simulate a signal, the heamodynamic response function of $h(t) = t^{8.6} e^{-t/0.547}$, with t as time in second, was added to the baseline time series. The amplitudes of signals were assumed to be 1% over the baseline. There are total of five defined active areas: two frontal, two posterior and one temporal regions. The simulated signal is based on a block design paradigm with period of 30 scans (Figure 1). Permutation tests with test statistic of mean difference the two conditions were applied to the dataset. The maximal null distribution was derived either with the iterative method, using the signals from the stimulated period and resting period (A and B in Figure 1), or with the proposed method using the signals from the resting period (A' and B in Figure 1). The results from the two approaches were then compared. The proposed method has better performance in terms of detecting power. All five regions were detected by the approach, whereas, only three regions were detected by the iterative approach. The extent of each detected region is also larger with the new method (Figure 2) while there is no voxel is incorrectly identified as active.

DISCUSSION

A new approach of constructing the maximal null distribution for permutation tests on neuroimaging data is proposed. The null distribution is constructed based on the data only from the control condition. This approach guarantees the derived null distribution contains few signals from any active voxel, and thus provides a less biased estimation of the distribution. Based on the simulation results, the approach could provide higher statistical power for detecting active regions. Furthermore, since there are no active voxels in the null distribution, the distribution is constructed in one step, and no iteration is required. The propose approach can improve the permutation test power while reducing the computation costs. Even there is no voxel incorrectly identified as active in the simulation, further studies are needed to investigate the Type I error control and the effect of substantial delay of BOLD response.

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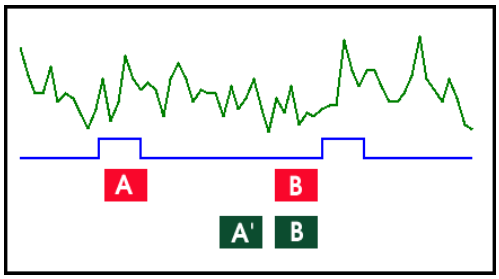

Figure 1. Segment of signal time course of an active voxel (green line), and the block design paradigm (blue line). The periods of two conditions used to generate the null distribution are shown in colour blocks, red (above) for iterative approach and dark green (below) for the proposed approach

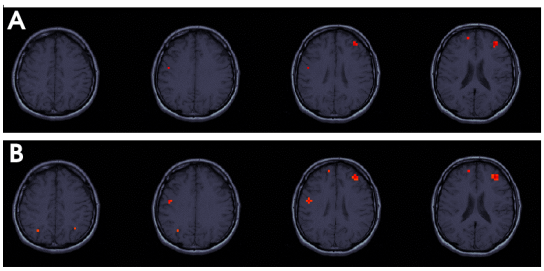

Figure 2. The detected active regions by the iteration approach (A), and the proposed approach (B).