



A Method for Improved Sensitivity and Flexibility of Psychophysiological Interactions in Event-Related fMRI Experiments

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INTRODUCTION

Psychophysiological interactions have been gaining widespread use in neuroimaging studies. Importantly, these studies identify connectivity patterns between brain regions that are task/condition-dependent. Despite their widespread use and utility in interpreting functional patterns on a systems level, these interactions have several limitations. First, they only identify task-dependent connectivity differences, not similarities. Secondly, they are limited to simple experiments with only two tasks. Here we present a novel variant of existing methods that address these limitations.

METHODS

Psychophysiological interactions were first developed in association with block designs [1] and later extended to event-related designs without considering the underlying sources of neural activity [2,3]. In a block design, there is typically an ON and OFF state, which means the neural activity has two possible states.



However, in an event-related design there are many more possibilities. For a single task, there is the state of the neurons when the stimulus is present and then another state when the stimulus is not present. For an event-related design with two tasks, there are at least 3 discrete neuronal states: (i) responding to stimulus for task 1; (ii) responding to stimulus for task 2; and (iii) neuronal activity while there is no stimulus present. The latter may be further divided, especially where the time between task 1 and 2 may be different from the time between 2 and 1.



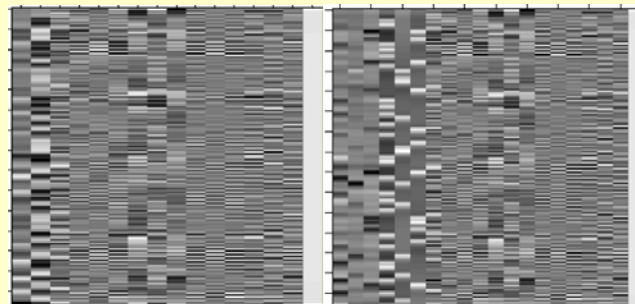
Our novel variant can account for many neuronal states.

$$Y_i = \text{conv}(\text{deconv}(Y_k) \times g_p) \beta_i + [Y_i \text{conv}(g_p) G] \beta_G + e_i$$

Although this equation is identical to the original equation, we have modified the input g_p , the psychological term, to contain multiple vectors, compared to a single vector consisting of a contrast weight times a stimulus vector.

Y_i is the signal from each voxel in the brain;
 Y_k is adjusted for the covariates of no interest (e.g. motion parameters, etc.);
 G is a matrix of the covariates of no interest;
 β_i and β_G are matrices of the beta estimates of their respective operands; and
 e_i is a vector of the residuals of model.

Original PPI Design Matrix Novel PPI Design Matrix



In the original and novel variant with 3 conditions, respectively: column 1 and columns 1-3 are the PPI term(s); column 2 and columns 4-6 are the psychological term(s); column 3 and column 7 are Y_k ; and the last 13 columns are covariates of no interest.

IMAGING

Recognition Memory of Neutral Faces

Twenty-eight adults (55 to 62 years old) underwent a fMRI paradigm consisting of an event-related task involving episodic recognition of gray-scale photographs of forward-facing, neutral faces. The task required participants to discriminate between previously viewed (PV) neutral faces from the training sets and novel (NV) neutral faces. In the encoding session prior to scanning, participants were instructed to view each face and respond with a key press regarding likeability or age of the face (greater than 25 years old), and to try to remember each face for a memory task that would be performed in the MRI scanner [4].

Recognition Memory of Trait Adjectives

Twenty-eight young adults (18 to 44 years old) participated in a fMRI paradigm consisting of an event-related task involving the episodic recognition of trait adjectives. The task required participants to discriminate between PV words from the training sets and NV words. In the encoding session prior to scanning, participants were instructed to view trait adjectives and respond with a key press regarding the question on the screen ("Does this word describe me?" or "Is the word positive?"), and to try to remember each word for a memory task that would be performed in the scanner.

fMRI Acquisition Parameters

All MR images were acquired on a GE 3.0 Tesla Signa (General Electric, Milwaukee, WI) with a standard quadrature head coil. BOLD imaging parameters were: echo time (TE) = 30 ms; repetition time (TR) = 2000 ms; flip angle = 90°; acquisition matrix = 64x64; field of view FOV= 240 mm. Thirty 4 mm thick sagittal slices with a 1mm gap were acquired within each TR. For the recognition of neutral faces, a 3D-field map was also collected [4].

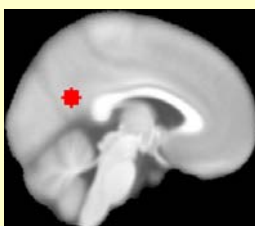
Image Analysis

BOLD images were slice time corrected, fieldmap corrected (if one was available), motion corrected, normalized to MNI space (EPI template), resampled to 2mm isotropic voxels, and smoothed with an 8mm FWHM Gaussian filter. Psychophysiological Maps were computed using the formula above using the Posterior Cingulate Cortex (PCC) as a seed region (below). The PCC region was a 10mm sphere centered at -4,-56,22. This was the peak coordinate in an independent study of self-appraisal. For the recognition of neutral faces, the two conditions were OLD and NEW. For the recognition of trait adjectives, there were three conditions: SELF OLD, SEMANTIC OLD, and NEW.

Statistical improvements were determined using the difference in the Akaike Information Criteria (AIC) from the novel variant and original method in a one-sample T-test.

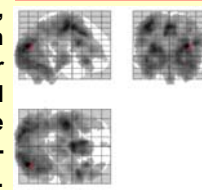
Paired T-tests evaluated which method revealed larger connectivity differences between conditions.

Individual tests within each method were computed. For the original PPI method, only the interaction term was tested. For the novel variant, all possible contrasts were computed (e.g single conditions as well as any differences between conditions (Self > Semantic).

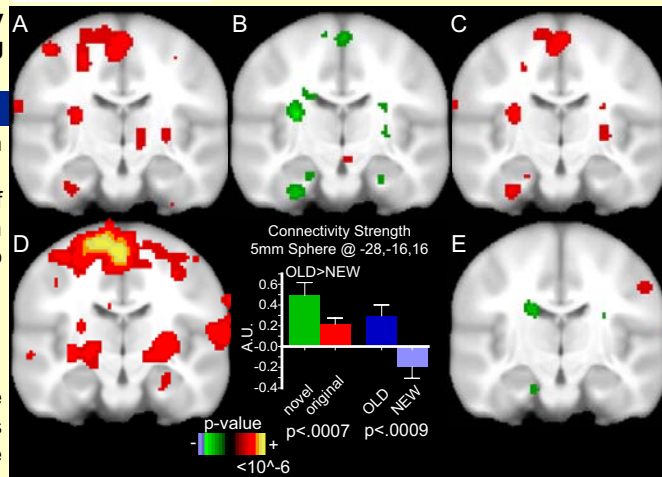


RESULTS

Recognition Memory of Neutral Faces

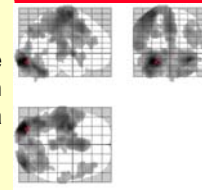


Maximum intensity projection showing areas of significant decreases ($p < .01$, unc; 20 voxels) in the AIC for the novel variant compared to the original PPI method.

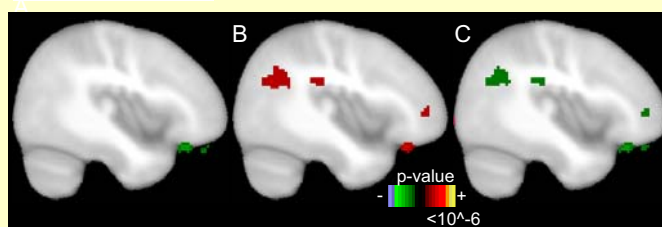


A coronal slice at $Y = -14.5$ showing statistical tests at $p < .01$ uncorrected in at least 20 connected voxels. A: Significant differences for OLD > NEW with the original PPI method. B: Significant differences for the original (red) > novel variant (green). C: Significant differences for OLD > NEW with novel variant. D: Significant connectivity in the OLD task. E: Significant connectivity in the NEW task. The maps for both methods are similar, however, the significance is increased in the novel variant. A couple of regions are lost; this is likely due to a better model of the data.

Recognition Memory of Trait Adjectives



Maximum intensity projection showing areas of significant decreases ($p < .01$, unc; 20 voxels) in the AIC for the novel variant compared to the original PPI method.



A sagittal slice at $x = -53.5$ showing where the connectivity strength for OLD items is greater than NEW items at $p < .01$ uncorrected in at least 20 voxels. A: Original method. B: Difference between the novel variant (red) and original method (green). C: Novel variant.

The OLD > NEW contrast was formed using weights of -2 (NEW), 1 (SELF OLD), and 1 (SEMANTIC OLD) for both methods. However, the interpretations are different (discussion).

A coronal slice showing a region of the parahippocampal gyrus where connectivity with the PCC differs between the SELF and SEMANTIC conditions. This result shows that the connectivity of two conditions can not be assumed to be equal.

DISCUSSION

- (1) The two methods are very similar, but the novel variant might be more sensitive.
- (2) The comparison of AIC for the two designs demonstrates that the novel variant is an improvement; whether this results from the additional psychological terms or psychophysiological terms is unknown and was not evaluated.
 - (a) A [-2 1 1] contrast for the original method means that one condition will have twice the negative amplitude than the other conditions (an assumption of relationship between conditions/tasks); while in the novel variant you multiply the amplitude by negative 2.
 - (b) The contrast for the original method has an impact on both the psychological and PPI terms, but not in the novel variant.
- (3) The novel variant allows researchers to explore specific conditions/tasks (e.g Old and New, Self and Semantic) and conjunctions of conditions/tasks.
- (4) The novel variant does not require a new computation of a new statistical model for each interaction that a researcher is interested in investigating.
- (5) Since inputs into the second-level analysis are the contrast images from the first level, there is no loss of power at the second-level.
- (6) Future investigations should explore multiple conditions in a block design.

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