Neural correlates of interspecies perspective taking in the post-mortem Atlantic Salmon: An argument for multiple comparisons correction

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INTRODUCTION

With the extreme dimensionality of functional neuroimaging data comes extreme risk for false positives. Across the 130,000 voxels in a typical fMRI volume the probability of a false positive is almost certain. Correction for multiple comparisons should be complete with these datasets, but is often ignore by investigators. To illustrate the magnitude of the problem we carried out a real experiment that demonstrates the anger of not correcting for chance properly.

METHODS

Subject. One mature Atlantic Salmon (Salmo salar) participated in the fMRI study. The salmon was approximately 18 inches long, weighed 3.8 lbs, and was not alive at the time of scanning.

Task. The task a ministor to the salmon involved completing an open-ended mentalizing task. The salmon was shown a series of photographs depicting human in ivi uals in social situations with a specific emotional valence. The salmon was asked to discriminate what emotion the in ivi ual in the photo must have been experiencing.

Design. Stimuli were presented in a block design with each photo presented for 10 seconds followed by 12 seconds of rest. A total of 15 photos were is playe . Total scan time was 5.5 minutes.

Preprocessing. Image processing was complete using SPM2. Preprocessing steps for the functional imaging data included a 6-parameter rigid-body affine realignment of the fMRI timeseries, coregistration of the data to a T₁-weighted anatomical image, and 8 mm full-width at half-maximum (FWHM) Gaussian smoothing.

Analysis. Voxelsewise statistics on the salmon data were calculated through an ordinary least-squares estimation of the general linear model (GLM). Predictors of the hemodynamic response were modeled by a boxcar function convolved with a canonical hemodynamic response. A temporal high pass filter of 128 seconds was applied.

Voxel Selection. Two methods were used for the correction of multiple comparisons in the fMRI results. The first method controlled the overall false discovery rate (FDR) and was based on a method defined by Benjamini and Hochberg (1995). The second method controlled the overall familywise error rate (FWER) through the use of Gaussian ran fiel theory. This was one using algorithms originally devised by Friston et al. (1994).

DISCUSSION

Can we conclude from this data that the salmon is engaging in the perspective-taking task? Certainly not. What can we determine is that ran on noise in the EPI timeseries may yield spurious results if multiple comparisons are not controlled for. Adaptive methods for controlling the FDR are excellent options and are widely available in all major fMRI analysis packages. We argue that relying on an statistical threshold (p < 0.001) is an ineffective control for multiple comparisons. We further argue that the vast majority of fMRI studies should be utilizing multiple comparisons correction as standard practice in the computation of their statistics.

REFERENCES


GLM RESULTS

A contrast was used to test for regions with significant BOLD signal change using the photo condition compared to rest. The parameters for this comparison were t(131) > 3.15, p(uncorrected) < 0.001, 3 voxel extent threshold.

Several active voxels were discovered in a cluster located within the salmon’s brain cavity (Figure 1, see above). The size of this cluster was 81 mm³ with a cluster-level significance of p = 0.001. Due to the coarse resolution of the echo-planar image acquisition an the relatively small size of the salmon brain further discrimination between brain regions could not be completed. Out of a search volume of 8064 voxels a total of 16 voxels were significant.

I empirical contrasts controlling the false discovery rate (FDR) and familywise error rate (FWER) were complete . These contrasts in icate no active voxels, even at relaxe statistical threshold s (p = 0.25).

VOXELSEWIZE VARIABILITY

To examine the spatial configuration of false positives we complete a variability analysis of the fMRI timeseries. On a voxel-by-voxel basis we calculate the standard deviation of signal values across all 140 volumes.

We observe clustering of highly variable voxels into groups near areas of high voxel signal intensity. Figure 2a shows the mean EPI image for all 140 image volumes. Figure 2b shows the mean EPI image of each voxel. Figure 2c shows thresholded EPI image overlaying the high-resolution T₁-weighted image.

To investigate this effect in greater detail we complete a Pearson correlation to examine the relationship between the signal in a voxel and its variability. There was a significant positive correlation between the mean voxel value and its variability over time (r = 0.54, p < 0.001). A scatterplot of mean voxel signal intensity against voxel voxel and evation is presente to the right.