Alternative Correction for Multiple Comparisons by Permutation

Recently, Eklund et al. (arXiv.org/pdf/1511.01863) have submitted for publication evidence that FWE-corrected cluster-size thresholds from Gaussian random-field Monte Carlo simulations are inaccurately lenient for fMRI. Our choice of primary threshold (p<0.001) and requirement that secondary locales be present in two family-wise error corrected connectivity maps likely reduces that concern for our findings. However, following their recommendations, we have also checked our results using permutation tests.

Because the main findings of interest are between two groups, an identical test to the multivariate group test may be constructed using 3dttest++ with the Motion Index as a covariate and effects coding for age category, group by age interaction, gender, and scanner assignment. The rapid processing of 3dttest++ allows for feasible testing of 5000 permutations of group. These group permutations were done within scanner assignment to maintain the balance of scanner across groups.

Here are the primary locales' percentiles in the distribution of maximum cluster size by random assignment of group:

Region	Contiguous Voxels	Percentile
Parietal	38	95.9
PCC	37	95.8
Temporal Pole	25	92.8
Precentral Gyrus	22	91.5

Of note, two of the locales are above the 95%ile and may be accepted by convention (P<.05). While the other two fail to meet the 95%ile criterion, they are above the 90%ile and constitute a statistical trend (P<.1). On this point, permutation-test controls such as this can be conservative, since random re-labeling of groups close to the original labeling is part of the estimated null distribution (e.g. Nichols, 2002, PMID 11747097).

Next, we determined how many of the original final set of locales reported in Table 2 of the manuscript may be selected via permutation testing. For this analysis, only the two primary locales above the 95%ile in permutation were selected. Next we ran permutation testing *across* the two group tests using each locale as a seed. In other words, on each iteration, we performed both seed tests and took the maximum cluster size in either seed test. Because the permutation test was done across the two tests, all clusters larger than the common 95%ile for either test may be selected. (Note, for the original locale selection, we had an additional requirement that secondary locales must be in at least two seed test results). Figures 1 and 2 demonstrate that almost all original voxels and all original locales would be selected at some permutation testing threshold.

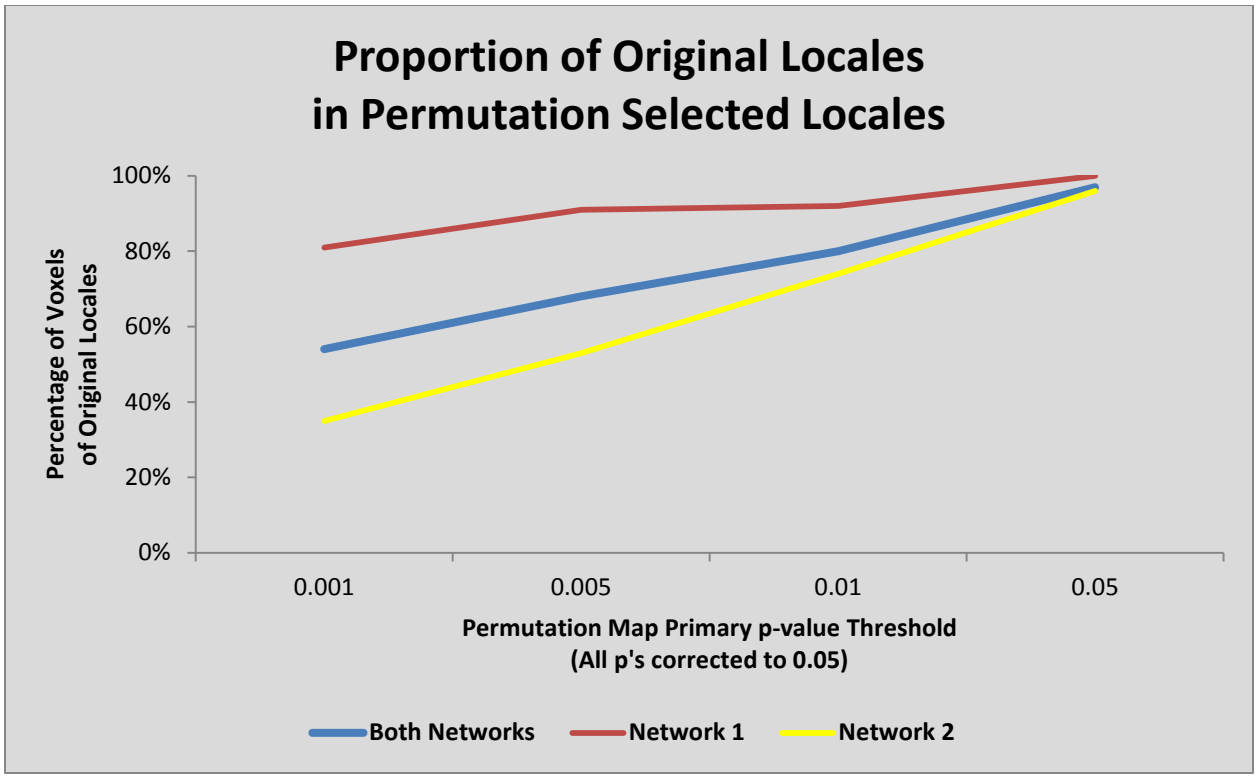

Figure 1. The percentage of voxels the final locales selected by Monte Carlo cluster correction, the original locales in the manuscript, within the final locales selected by permutation testing.

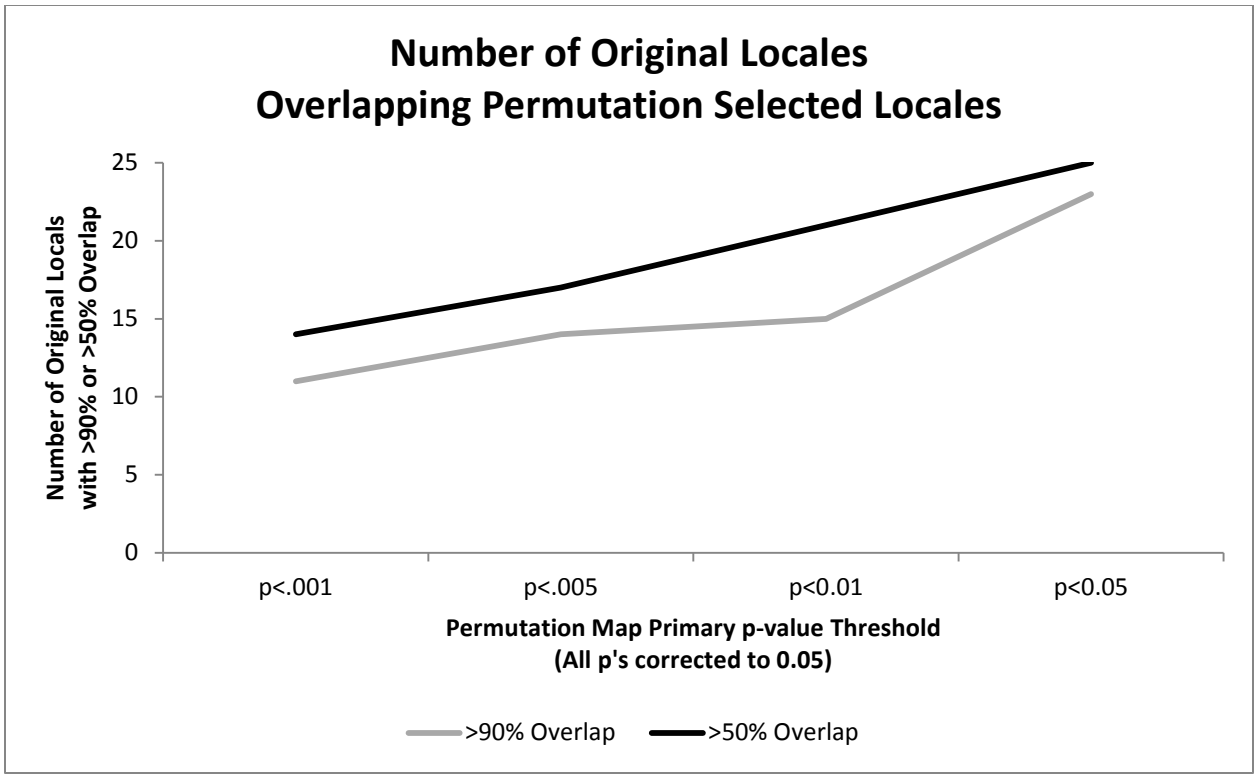

Figure 2. The number of final locales selected by Monte Carlo cluster correction, the original locales in the manuscript, overlapping by 50% or more within the final locales selected by permutation testing.