Alternative-Based Thresholding: A Simulation Study

Jasper Degryse[a], Ruth Seurinck[a], Joke Durnez[a] and Beatrijs Moerkerke[a]

[a] Department of Data Analysis, Ghent University, Belgium

UNIVERSITEIT GENT

fwo Research Foundation Flanders Opening new horizons

1. Functional Regions of Interest (fROI)

Advantages & applications:

- Increased sensitivity[1]
- Input for further hypothesis testing: connectivity, TMS, biomarker,...

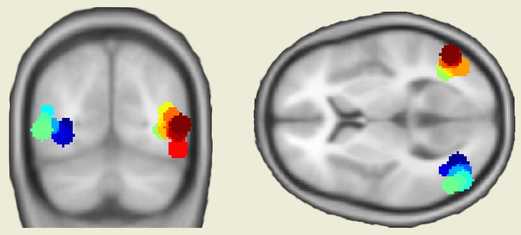

Figure 1 : Example of an fROI (left = coronal, right = axial). Identifying hMT/V5+ in 9 subjects[4].

2. fROIs and thresholding

- We still need to correct for multiple testing in fROI (e.g., FWE, FDR,...): the chance on a false positive (FP) increases with the the number of voxels tested.
- We want to avoid both FP and false negatives (FN) (see Figure 2).
- Current thresholding only focuses on avoiding FP by testing against H_0 (0 % BOLD signal change).
- FP rate is controlled directly, but not the FN rate. However, thresholding induces a trade-off between FP and FN.
  - Lenient threshold: increase in FP and decrease in FN[1]
  - Stringent threshold: decrease in FP and increase in FN[1]
  - More FP $\Rightarrow$ overestimation
  - More FN $\Rightarrow$ underestimation

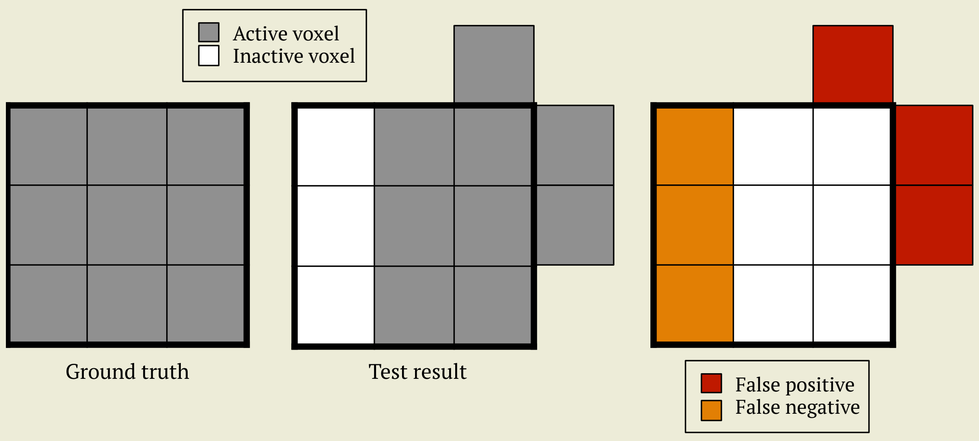

Figure 2 : Illustration of FP, or overestimation, and FN, or underestimation, in the test result with respect to the ground truth.

3. Alternative-based thresholding procedure (ABTP)[2]

- Test against both H_0 and H_1[2] to control both FP and FN rate.
- H_1 is specified by Δ_1, the magnitude of the effect (in % BOLD signal change) expected under true activation, with $\Delta_1 \sim \mathcal{N}(\mu_{\Delta_1}, \tau^2)$[2].
- The procedure leads to two measures of evidence: classical p-value p_0 and alternative p-value p_1.
- The combination of thresholding these p-values ($p_0 \leq \alpha$; $p_1 \geq \beta$) results in a layered statistical parametric map (LSPM) with four layers.

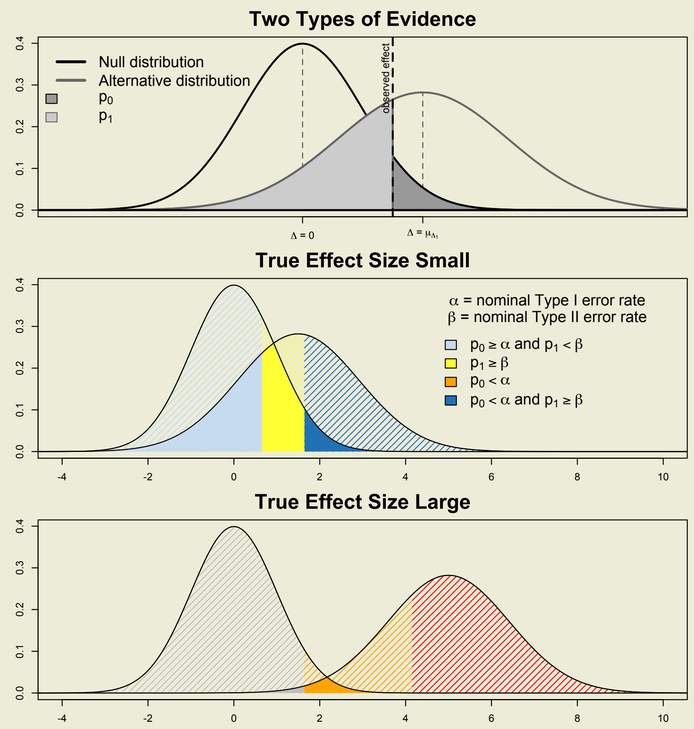

Figure 3 : Visualization of p_0 and p_1 (top), and of the different types of voxels or layers (middle & bottom).

p_0: the smaller, the more evidence against H_0

p_1: the smaller, the more evidence against H_1

Active: strong evidence against null of no activation

Inactive: activity confidently excluded

Uncertain: activity not confidently excluded

Practically Insignificant: activity not clinically significant

4. Method simulations

- 500 single subject data sets (resolution: 30×30×30; isotropic voxels: 1mm; sphere)
- 600 scans, TR of 2s
- Blocked ON/OFF design, 20s/block
- Smoothed with FWHM of 6mm
- Gaussian white noise added
- Classic testing: FDR correction at 0.05
- Manipulated parameters (ABTP): true underlying effect size, contrast to noise ratio, α, β and τ

5. Results

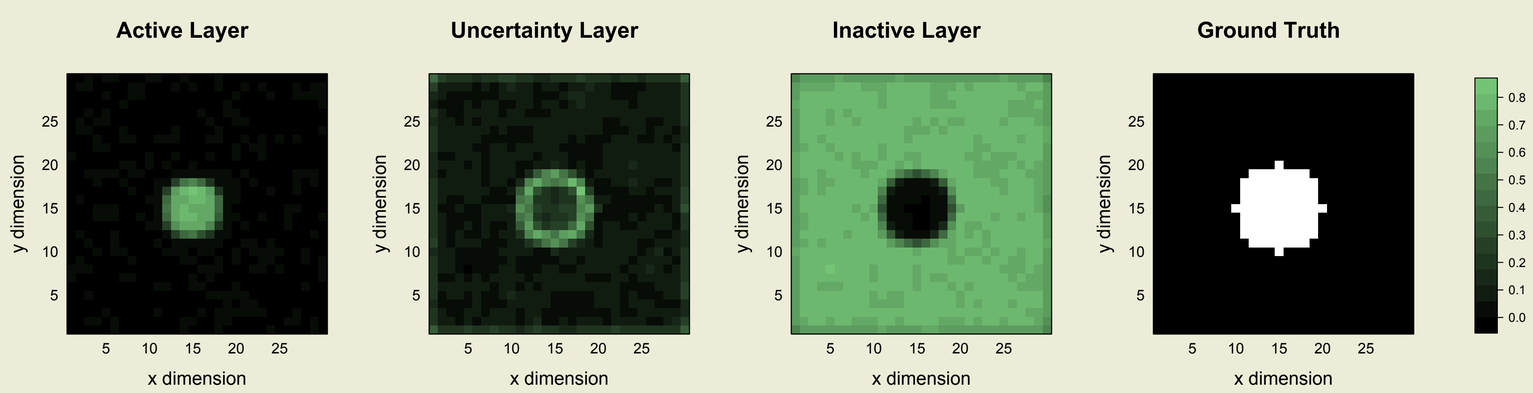

Figure 4 : Visual presentation of the LSPM. The greener the voxel is, the more it occurred in the layer that is shown over all simulations.

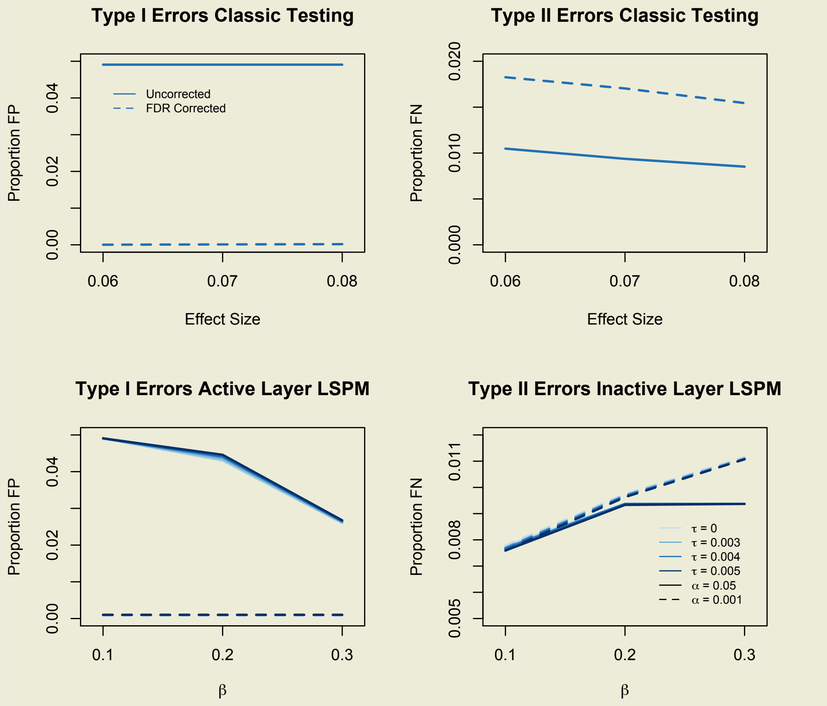

Figure 5 : False positives (Type I errors) and False negatives (Type II errors) for both the classic testing procedure and the ABTP.

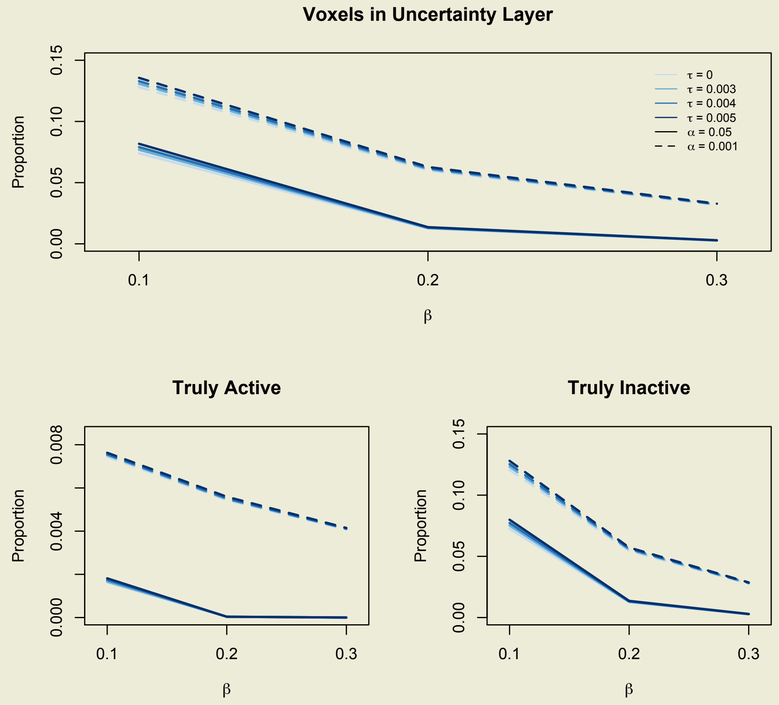

Figure 6 : The number of voxels in the uncertainty layer (above) that are truly active (left bottom) or truly inactive (right bottom).

6. Discussion & conclusions

- The number of FP in the LSPM corresponded with uncorrected testing with $\alpha = .05$, but dropped to that of the FDR corrected testing when $\alpha = 0.001$.
- Importantly, the overall number of FN in the LSPM was lower than in both the uncorrected and FDR corrected classic testing procedure.
- With increasing β or decreasing τ, the number of FN increased and the number of FP decreased.
- The uncertainty layer consisted of more voxels as α and β decreased and τ increased. The number of truly inactive voxels in this layer was consistently larger than the number of truly active voxels for all parameter values.

Conclusions

1. The greatest advantage in using the ABTP is the decrease of FN, compared to both the uncorrected and FDR corrected classic testing methods.
2. When α and β are adjusted appropriately, the number of FP can also be reduced.

7. References

[1] Duncan & Devlin, (2011). *Neuroimage, 57*
[2] Durnez, Moerkerke, Bartsch, & Nichols (2013). *CABN, 13*
[3] Nieto-Castanon, & Federenko (2012). *Neuroimage, 63*
[4] Seurinck, de Lange, Achten & Vingerhoets (2011). *JCN, 23*