

Localized Cluster Enhancement: TFCE revisited with valid error control

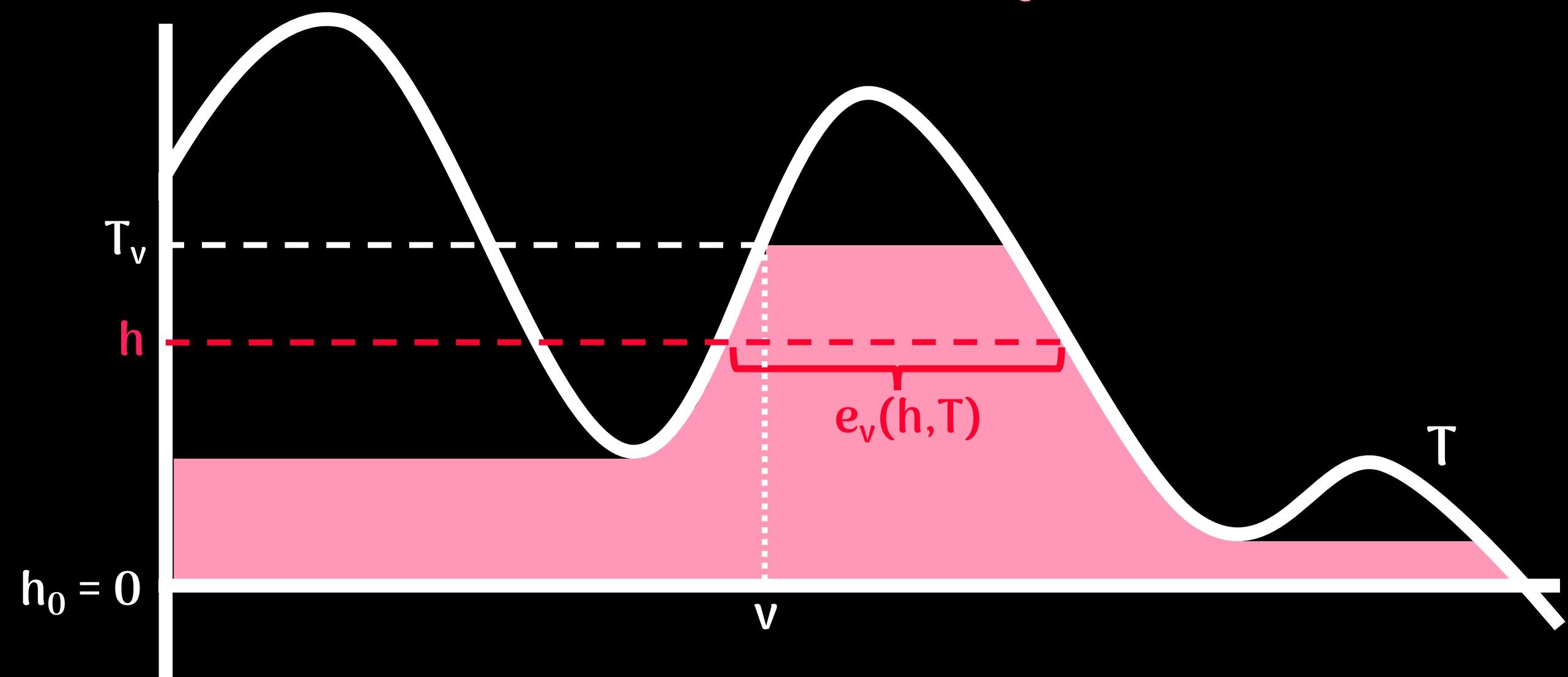


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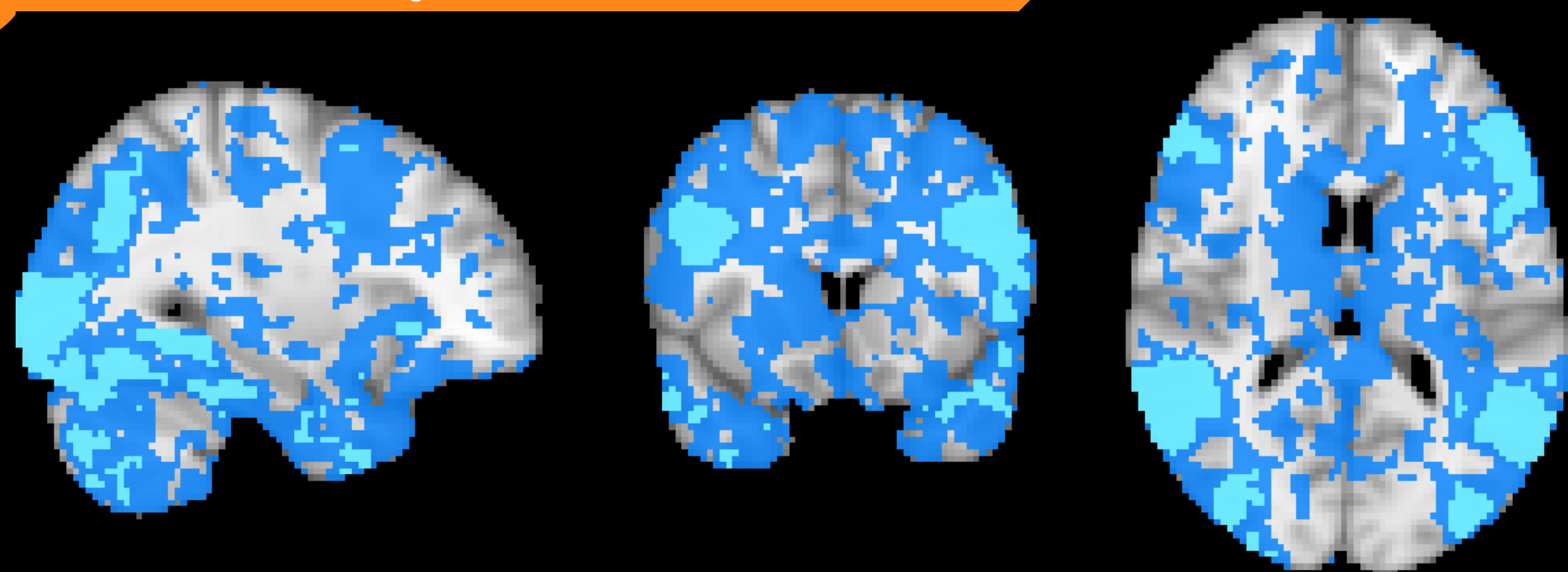
1 Understanding TFCE

$$S_v(T) = \int_{h_0}^{T_v} h^H e_v(h, T)^E dh$$



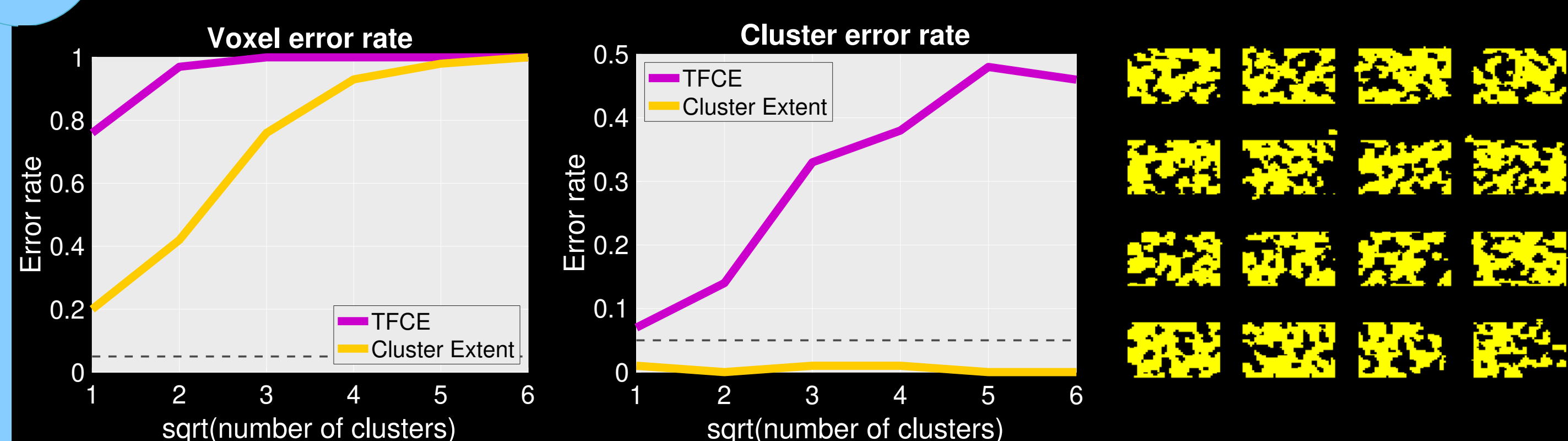
In the TFCE approach a threshold t^* is computed based on the $1 - \alpha$ quantile of the permutation distribution of $\max_{v \in V} S_v(T)$. Voxels v with $S_v(T) > t^*$ are returned.

2 TFCE has poor localization



TFCE significant clusters shown in light blue, the true support is shown in dark blue, and covers half the brain. This shows that the localization ability of TFCE is very bad. Moreover it shows that TFCE depends very strongly on the threshold h_0 as this determines the support. As such TFCE is not in fact threshold free despite its name. Data: 20 subjects from the HCP Social contrast

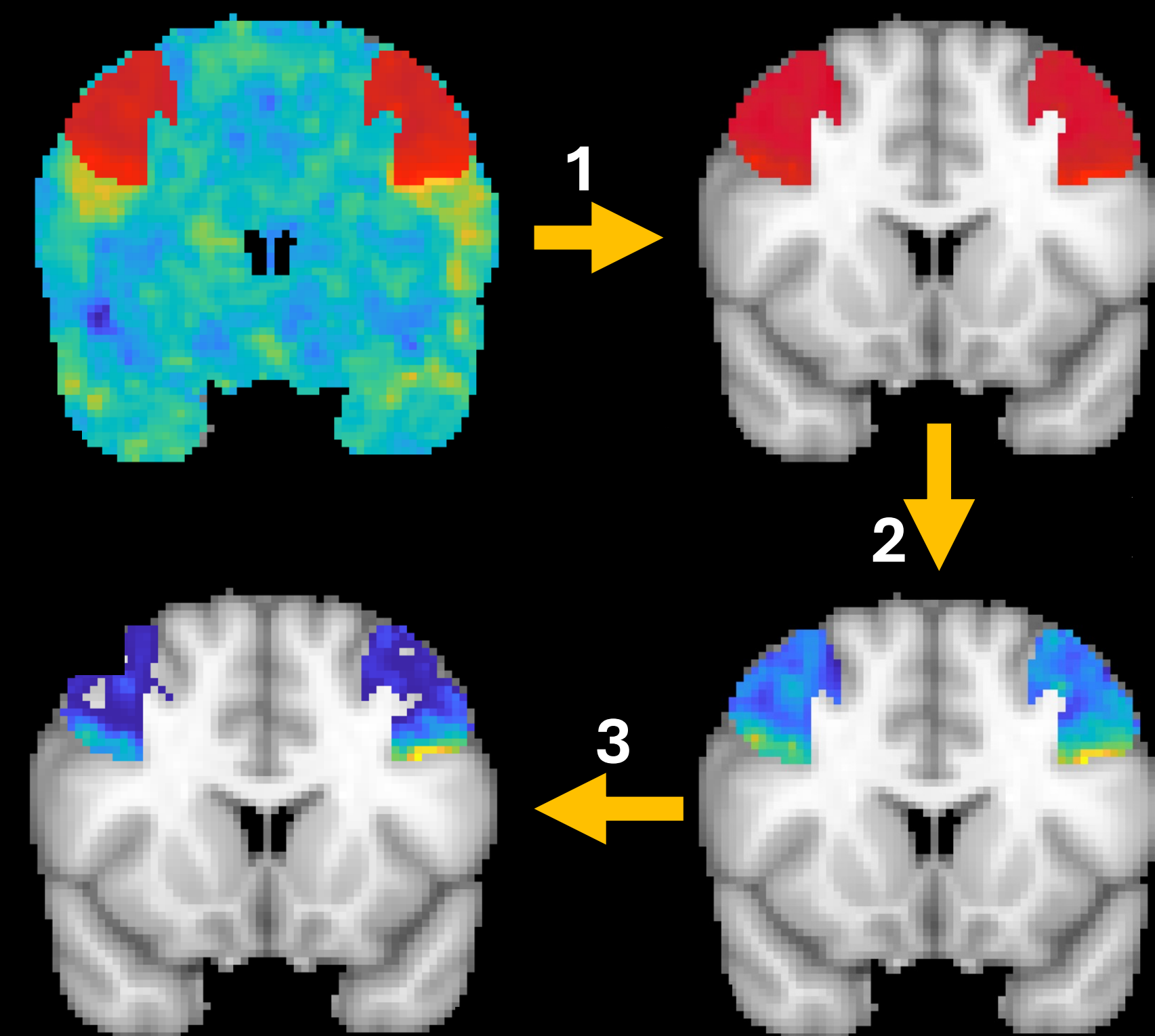
3 TFCE can have Inflated Error rates



We run simulations in order to check the voxelwise and clusterwise error rate of TFCE. TFCE is often interpreted voxelwise but this gives rise to very large false positive rates. However TFCE also has inflated clusterwise error rates due to cluster leakage. Here simulations consisted of generating 30 subjects by adding smooth Gaussian random noise to a many cluster mean. Right: example simulation.

4 Localized Cluster Enhancement (LCE)

To solve these issues we introduce LCE. Given a region R , LCE computes $S_v(T1[R])$ and rejects the null within R if this exceeds the threshold t^* . This is illustrated with an example region to the right. This amounts to applying a mask to the original test-statistic T , computing the TFCE statistic within that region and then comparing this to the threshold



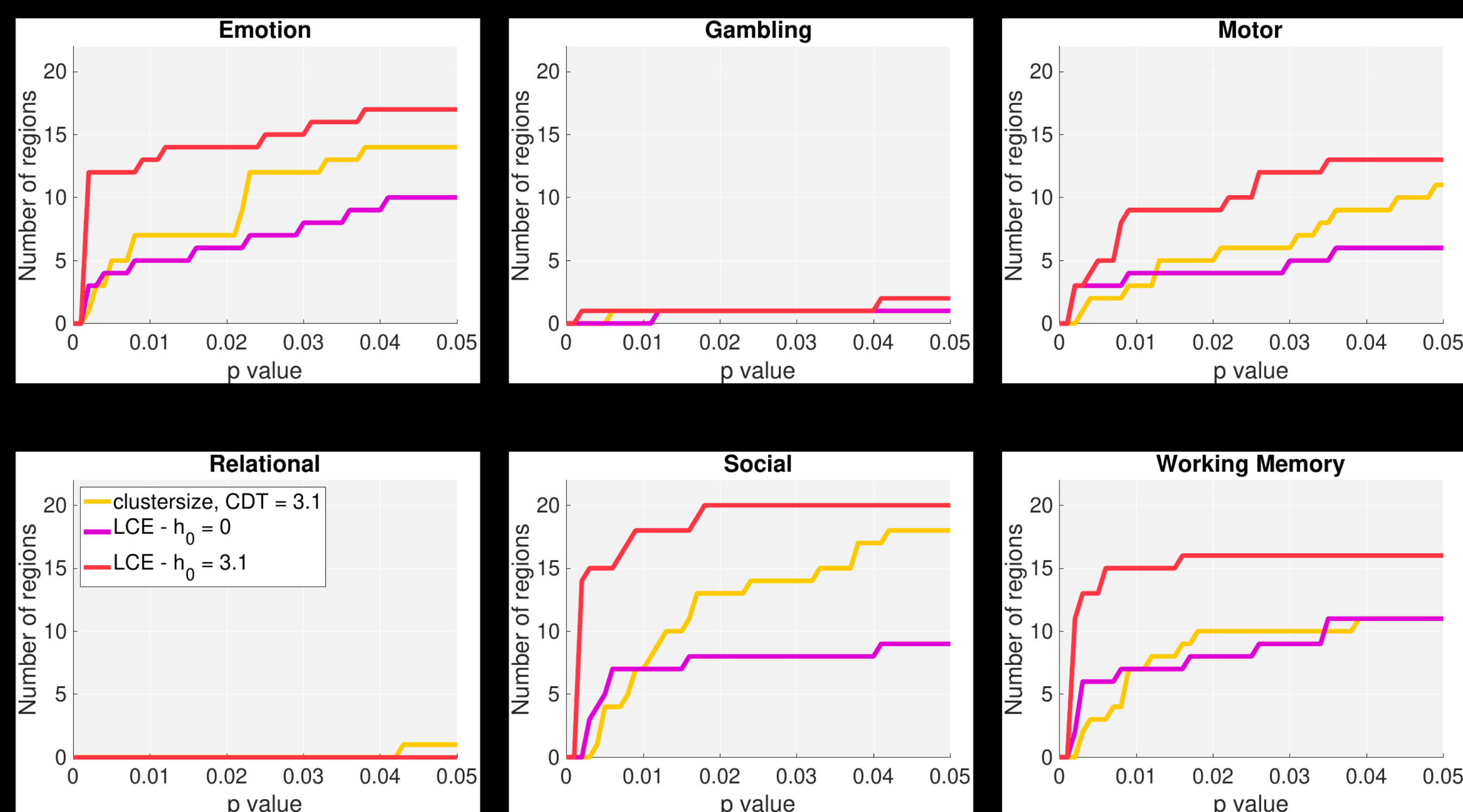
5 LCE Theory

We can formally prove that LCE contains regional error rates. In particular suppose that the data satisfies the permutation assumption, then

Theorem: $\mathbb{P}(S_{v,R}(T) < t^* \text{ for all inactive } R) \geq 1 - \alpha$

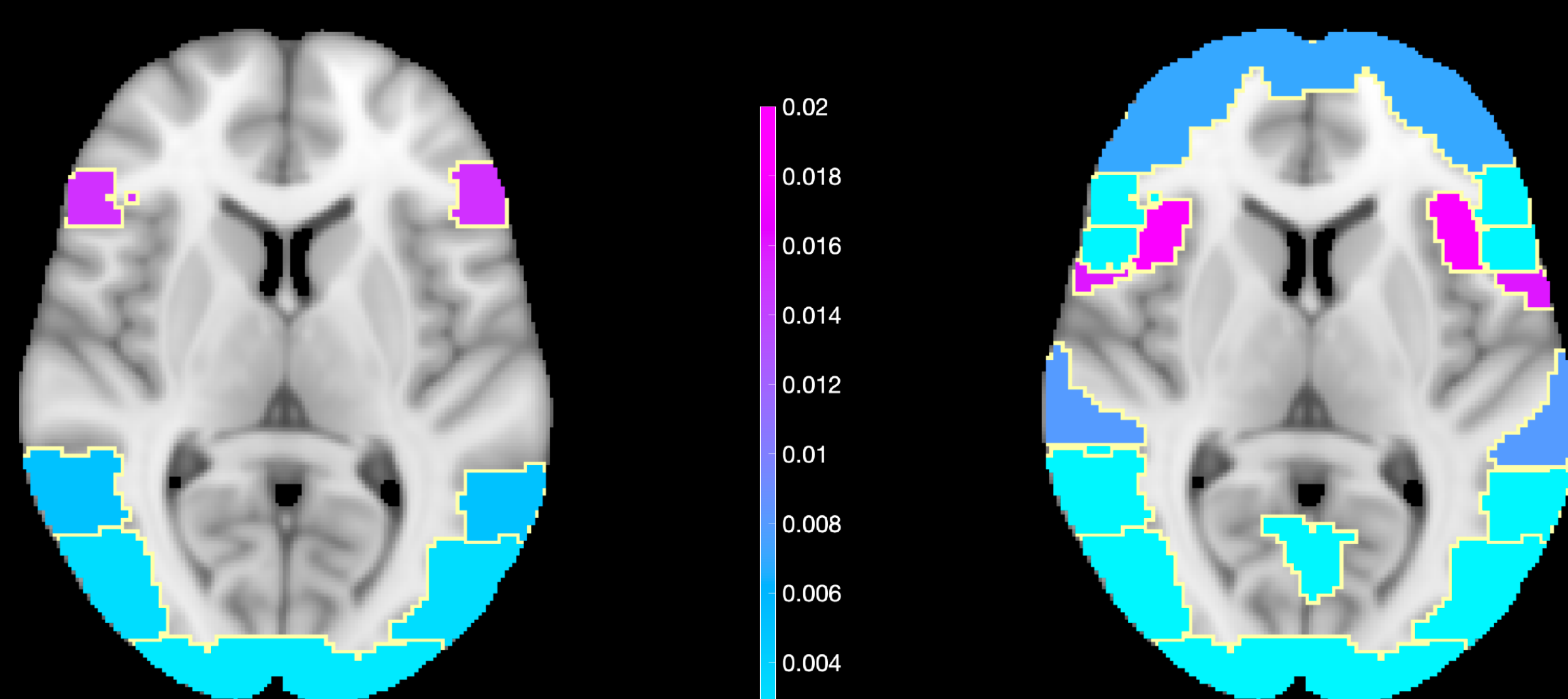
This result holds simultaneously over all inactive regions R . These can be anatomical ROIs or data-driven areas such as excursion sets. The simultaneous guarantee allows the user to search over multiple regions without worrying about data hacking.

6 LCE Regional Power on HCP tasks



We apply LCE with $h_0 = 0$ and $h_0 = 3.1$ and compare to the results of embedding clustersize inference into a closed testing procedure (as in Goeman 2023). We take groups of 20 subjects for the main 6 contrasts from the HCP dataset and perform a one-sample test. We see that taking $h_0 = 0$ is suboptimal typically producing the least power and usually in fact being less powerful than clustersize inference. Instead taking $h_0 = 3.1$ allows for a significantly more sensitive procedure which is more powerful than clustersize.

7 Increasing the threshold increases power



(a) Localized TFCE, $h_0 = 0$

(b) Localized TFCE, $h_0 = 3.1$

Application of LCE to a test of the social contrast from 20 subjects from the HCP. P-values for each region of the Harvard-Oxford cortical atlas were calculated using LCE. Right LCE with $h_0 = 0$, left LCE with $h_0 = 3.1$.

8 Discussion

- TFCE as used cannot be relied upon to control false positives.
- Localized Cluster Enhancement provably controls clusterwise and regional error rates and allows for increases in power and localization
- TFCE is not threshold free as it (strongly) depends on a threshold h_0 . The default choice of $h_0 = 0$ means that TFCE typically can only reject the global null.
- For localized cluster enhancement we recommend a threshold of $h_0 = 3.1$ in line with the default for clustersize inference.

9 StatBrainz

Matlab software to implement these methods is available online in the StatBrainz MATLAB package accessible at: www.github.com/sjdavenport/StatBrainz. A matlab LCE tutorial is available.



10 References

Smith, Stephen M., and Thomas E. Nichols. "Threshold-free cluster enhancement." *Neuroimage* (2009).
Goeman, Jelle J., et al. "Cluster extent inference revisited: quantification and localisation of brain activity." (2023)

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