

# Localized Cluster Enhancement: TFCE revisited with valid error control

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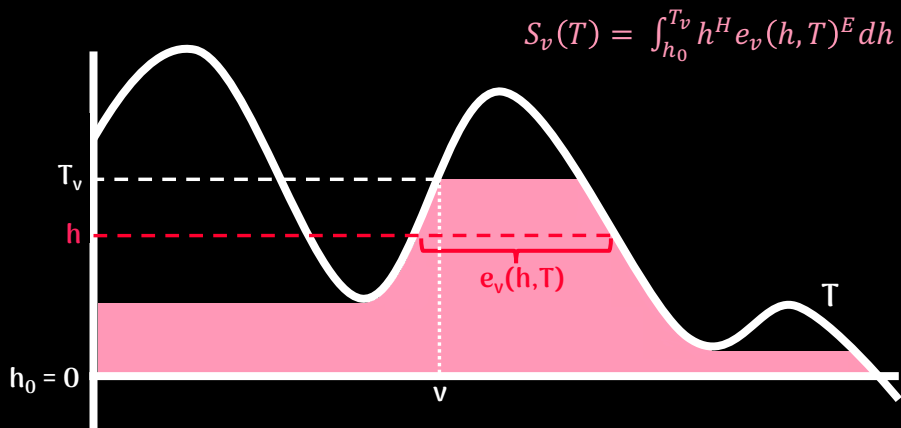
# TFCE recap

- Suppose that we want to test for activation using a test-statistic  $T : \mathcal{V} \rightarrow \mathbb{R}$  at each voxel in the brain.
- TFCE is a widely used method for identifying activation with over 5000 citations.
- At each voxel  $v$ , TFCE transforms  $T$  to

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

- Here  $h$  is the height and  $e_v(h, T)$  is the extent of the test statistic at the level  $h$  for the voxel  $v$ .

# Understanding the TFCE integral



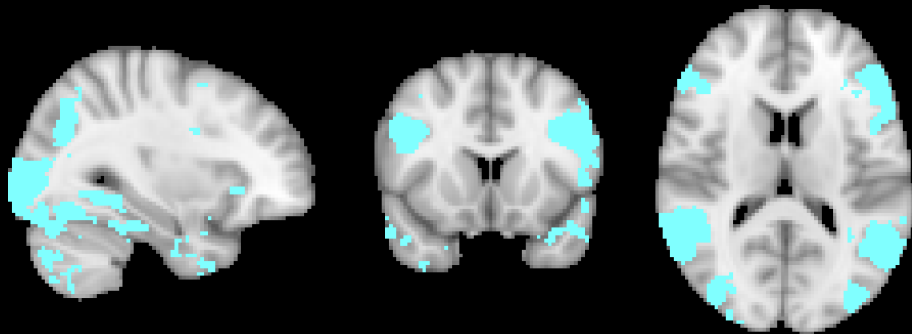
# TFCE recap

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

- In practice -  $H = 2$ ,  $E = 0.5$  and  $h_0 = 0$  are the default parameters typically chosen.
- Permuted TFCE test-statistics:  $S_{v,1}^*, \dots, S_{v,P}^*$  are calculated.
- cutoff  $t^*$  chosen based on the 95% quantile of the permutation distribution of  $\max_{1 \leq p \leq P} S_{v,p}^*$ . Reject  $v$  such that  $S_v(T) > t^*$ .

# Thresholded TFCE

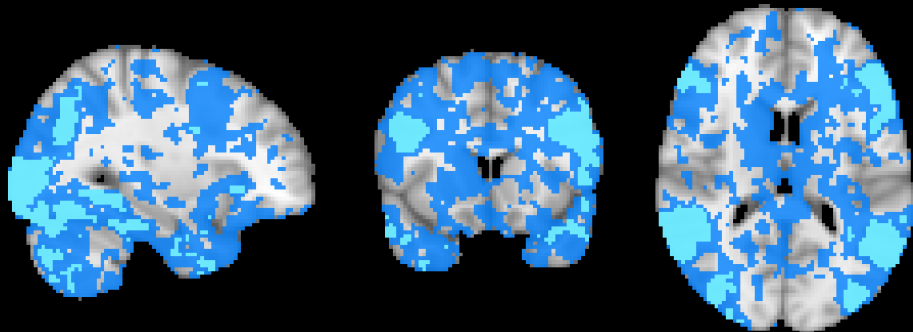
We apply TFCE to 20 subjects from the HCP to the primary social contrast.



However TFCE borrows information from across its support.

# TFCE support

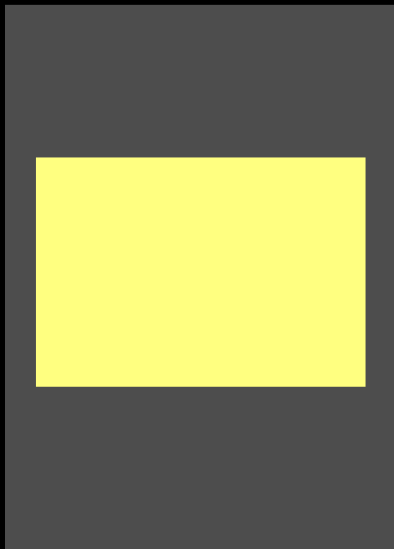
We apply TFCE to 20 subjects from the HCP to the primary social contrast.



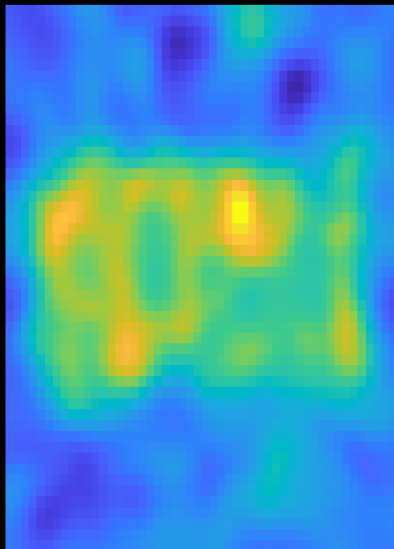
TFCE thus can be used to make a global statement but struggles to localize activation.

# Simulation example (based on $n = 50$ )

**Signal**

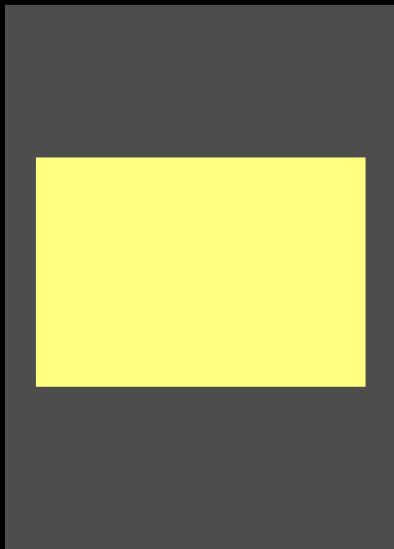


**t-statistic**

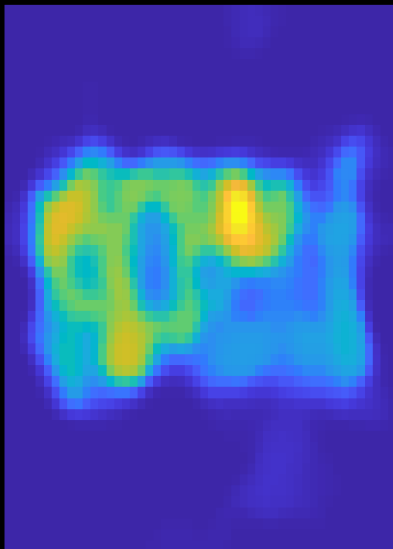


# Simulation example (based on $n = 50$ )

**Signal**



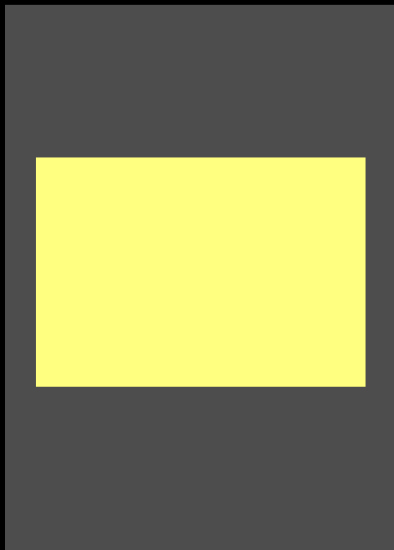
**tfce-statistic**



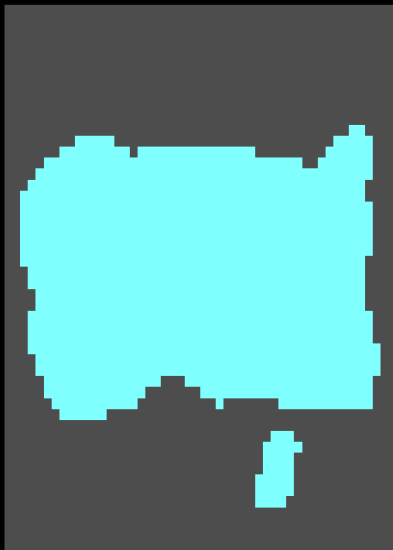


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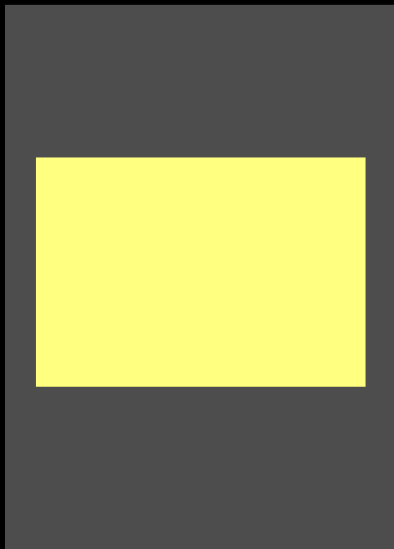


**Thresholded TFCE**



# Simulation example (based on $n = 50$ )

**Signal**

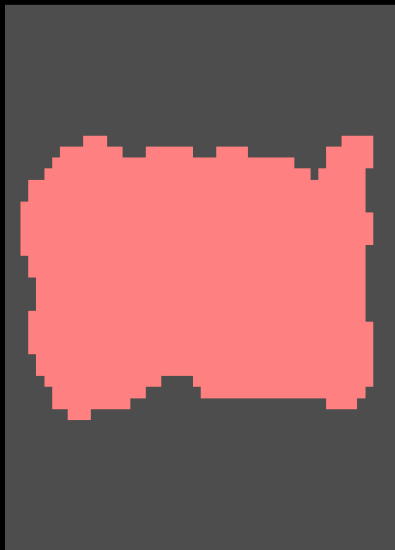


**TFCE support**



# Simulation example (based on $n = 50$ )

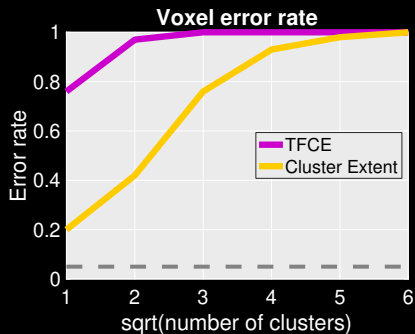
## Clustersize Inference



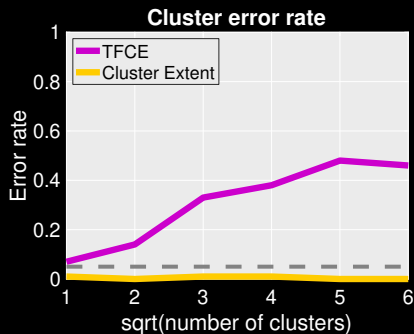
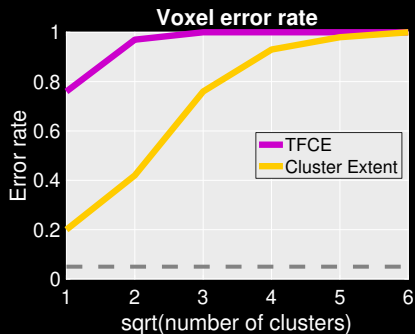
## Thresholded TFCE



# TFCE can have inflated error rates



# TFCE can have inflated error rates



- TFCE was designed to improve on cluster extent inference however it doesn't control cluster error rates
- One of the main motivations for TFCE was to reduce researcher degrees of freedom, to make it "threshold free". However the TFCE transformation is defined as:

$$S_v = \int_{h_0}^{T_v} h^H e_v(h)^E dh. \quad (1)$$

- In particular  $h_0$  acts as a threshold so TFCE is not threshold free.

# Localized Cluster Enhancement

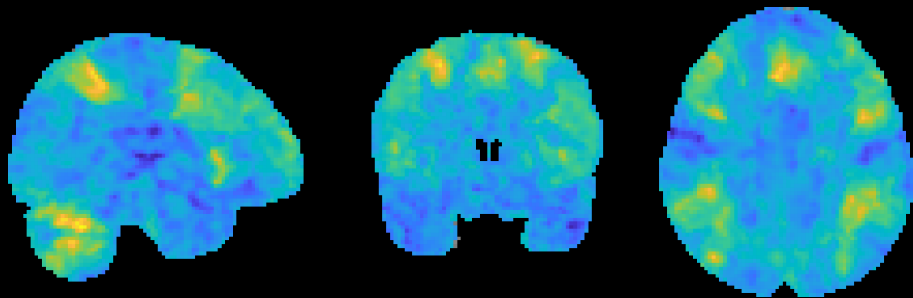
To localize TFCE for a region  $R \subset \mathcal{V}$  let

$$S_{v,R}(T) = S_v(T \times 1[R]) = \int_{h_0}^{T_v} h^H e_v(h, T \times 1[R])^E dh.$$

Then we can say  $R$  contains at least one active voxel if  $\max_{v \in R} S_{v,R}(T) > t^*$  where  $t^*$  is the original TFCE cutoff.

# Localized Cluster Enhancement illustration

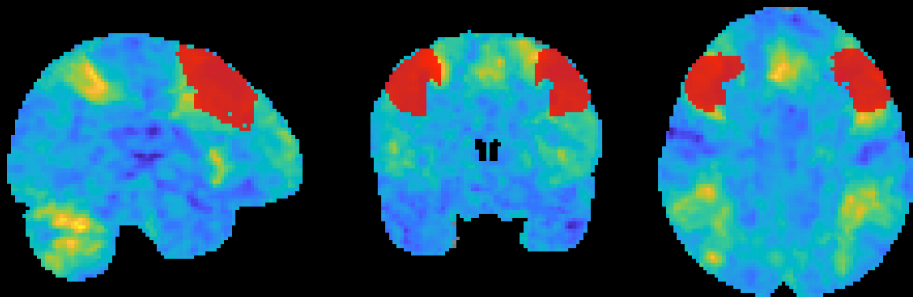
The  $t$ -statistic based on 20 subjects (for the HCP Gambling task)





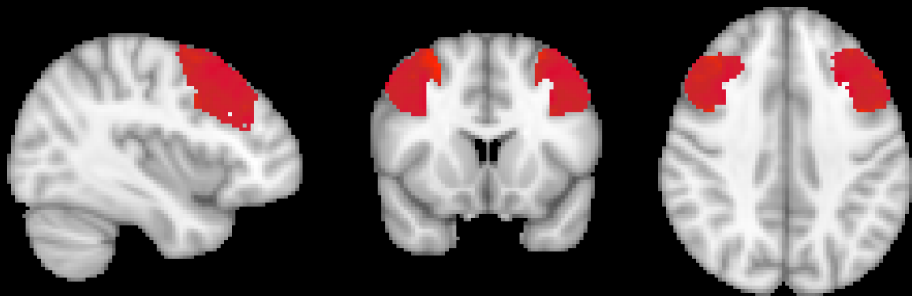
# Localized Cluster Enhancement illustration

Apply a mask of the Middle Frontal Gyrus



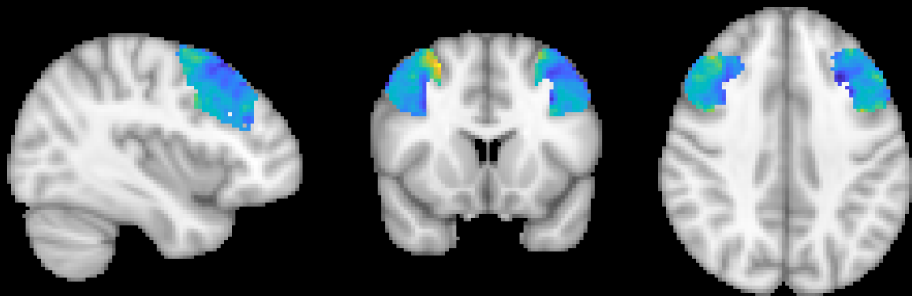
# Localized Cluster Enhancement illustration

Apply a mask of the Middle Frontal Gyrus



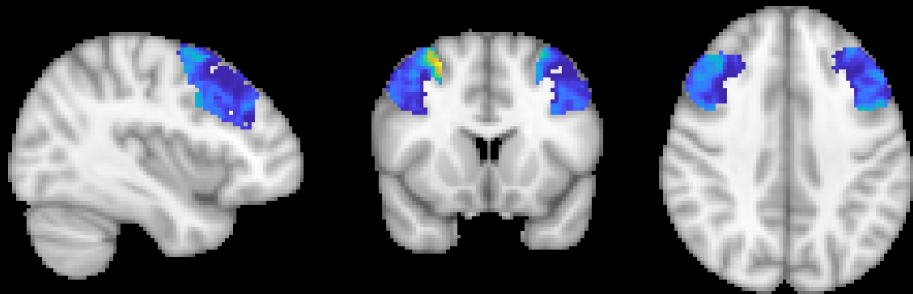
# Localized Cluster Enhancement illustration

Apply a mask of the Middle Frontal Gyrus



# Localized Cluster Enhancement illustration

Apply TFCE transformation to obtain  $\max_{v \in R} S_{v,R}(T)$

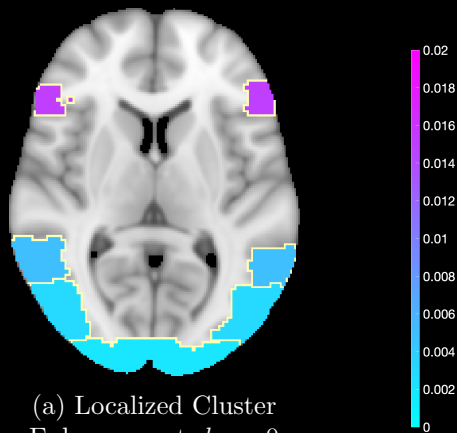


Reject if  $\max_{v \in R} S_{v,R}(T) > t^*$ .

# Advantages of Localized Cluster Enhancement

- If  $\max_{v \in R} S_{v,R}(T) > t^*$ , then LCE claims that there is at least one active voxel within the region  $R$ .
- This is provably valid (with an error rate of 5%) simultaneously over all regions  $R$  so LCE can make local claims unlike TFCE.
- LCE can be applied to pre-defined regions based on an atlas or to data-driven regions such as clusters.
- Allows the user to explore the data and find the regions  $R$  of interest.

# Regional activation (HCP - Social)

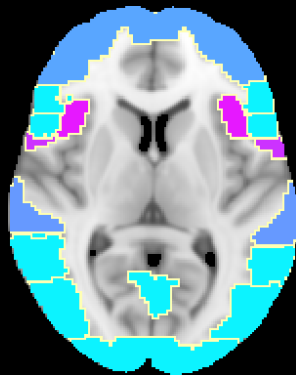


(a) Localized Cluster  
Enhancement,  $h_0 = 0$

# Regional activation (HCP - Social)



(a) Localized Cluster Enhancement,  $h_0 = 0$



(b) Localized Cluster Enhancement  $h_0 = 3.1$

# Conclusions

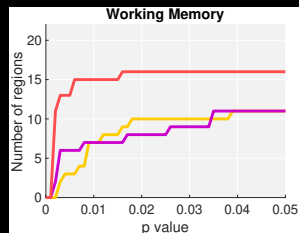
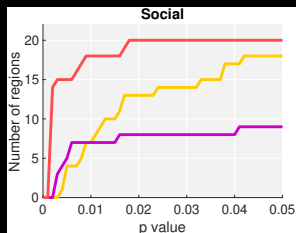
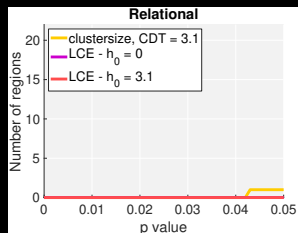
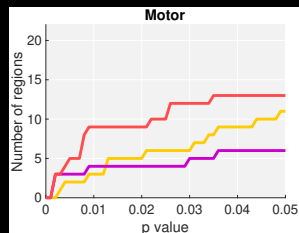
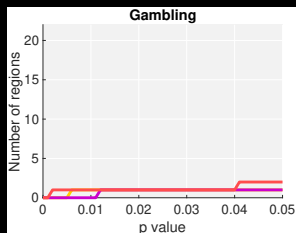
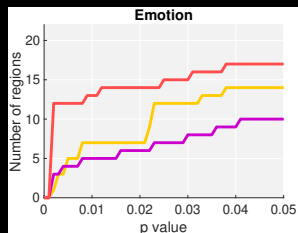
- TFCE as classically used can have inflated voxel and clusterwise error rates.
- **Localized Cluster Enhancement** provably controls clusterwise and regional error rates and allows for increases in power and localization.
- TFCE is not threshold free as it (strongly) depends on a threshold  $h_0$ . The default choice of  $h_0 = 0$  means that TFCE typically can only make the weak global statement in practice.
- For localized cluster enhancement we recommend a threshold of  $h_0 = 3.1$  in line with the default for clustersize inference.



# Thanks

- Slides for this talk are available on my website:  
`sjdavenport.github.io/talks`
- Code to implement LCE and a tutorial on TFCE are available in the StatBrainz MATLAB package available at:  
`sjdavenport.github.io/software`
- Further details available at my poster: 1871

# Power comparison for a regional analysis



Suppose that the data satisfies an exchangeability assumption. Then

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

# Global vs voxel vs cluster level inference

There are 3 types of inference statements typically used.

1. Voxel: Every highlighted voxel is active
2. Cluster: Every cluster contains at least one active voxel
3. Global: There is some voxel active somewhere in the brain.

# Classifying fMRI inference methods

There are 3 types of inference statements typically used.

1. Voxel: Every highlighted voxel is active

**Voxelwise inference**

2. Cluster: Every cluster contains at least one active voxel

**Clustersize inference**

3. Global: There is some voxel active somewhere in the brain.

**TFCE**