An antidote to the imager's fallacy, or how to identify brain areas that are in limbo

Gilles de Hollander[1,2], Eric-Jan Wagenmakers[2], Lourens Waldorp[2], Birte U. Forstmann[1,2]

1 Amsterdam Brain and Cognition Center, University of Amsterdam, the Netherlands, 2 Psychology Department, University of Amsterdam, the Netherlands

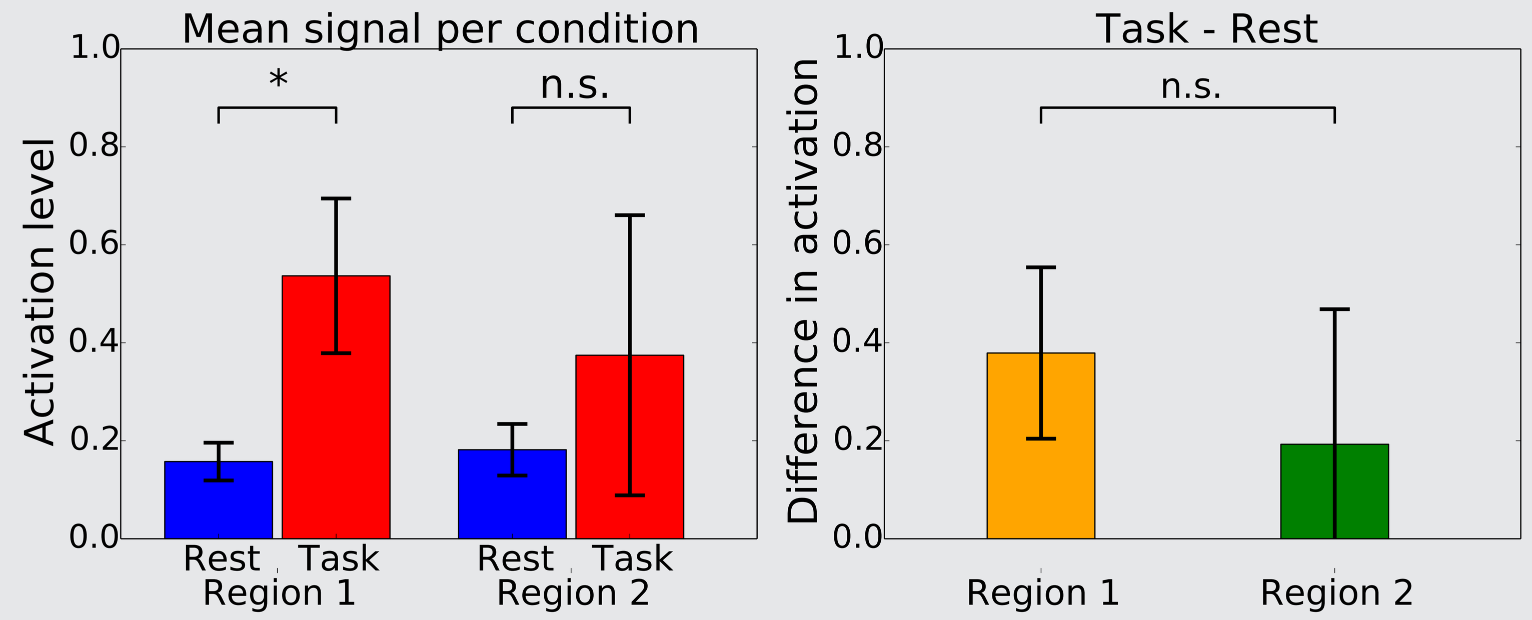
G.deHollander@uva.nl

The Imager's Fallacy

- The **Imager's Fallacy** (Henson, 2005) refers to the invalid inference that an area is *specifically* involved in some task, because an experimental contrast reaches a statistical threshold in that area, but does not in other areas.
- However, *the difference between significant and not significant is itself not necessarily significant* (Gelman & Stern, 2006).
- Instead of considering the **difference in p-values**, we should consider the **p-value for the difference**.

Example Imager's Fallacy

- Region 1 shows a significant difference in activation between a rest and task condition. Region 2 does not.
- However, the difference in activity between rest and task condition in Region 1 is not significantly different from the condition difference in activity in Region 2.



- The conclusion that Region 1 is specifically involved can not be drawn.

The In Limbo Approach

- **Solution to the imager's fallacy**: Test the contrast size of the *least-reliably significantly activated voxel* (the "comparison voxel") against the contrast size in all *non-significantly activated voxels*. This subdivides non-significantly activated regions into two categories:
  1. Areas in which the condition difference is significant are **reliably not activated**.
  2. Areas in which the condition difference is *not* significant are labeled **in limbo**: they are not significantly activated, but not significantly *less* activated than areas that are significantly activated either. The specificity of significantly activated areas remains unclear and more measurements should be made.

Steps of The In Limbo Approach

The approach consists of 4 steps:

1. **Estimate contrasts** and variances over the conditions. A general linear model (GLM) is fitted in every voxel using the sandwich estimator (Waldorp, 2009). The sandwich estimator is robust against autocorrelation and misspecification of the HRF.
2. **Threshold** the statistical parametric mapping. The resulting statistical parametric mapping is thresholded at some z-value, correcting for multiple comparison using gaussian random field theory (GRF).
3. Determine **the comparison voxel**. The voxel with the lowest z-value that is still significantly activated is chosen as a comparison voxel.
4. Determine regions that are **in limbo**

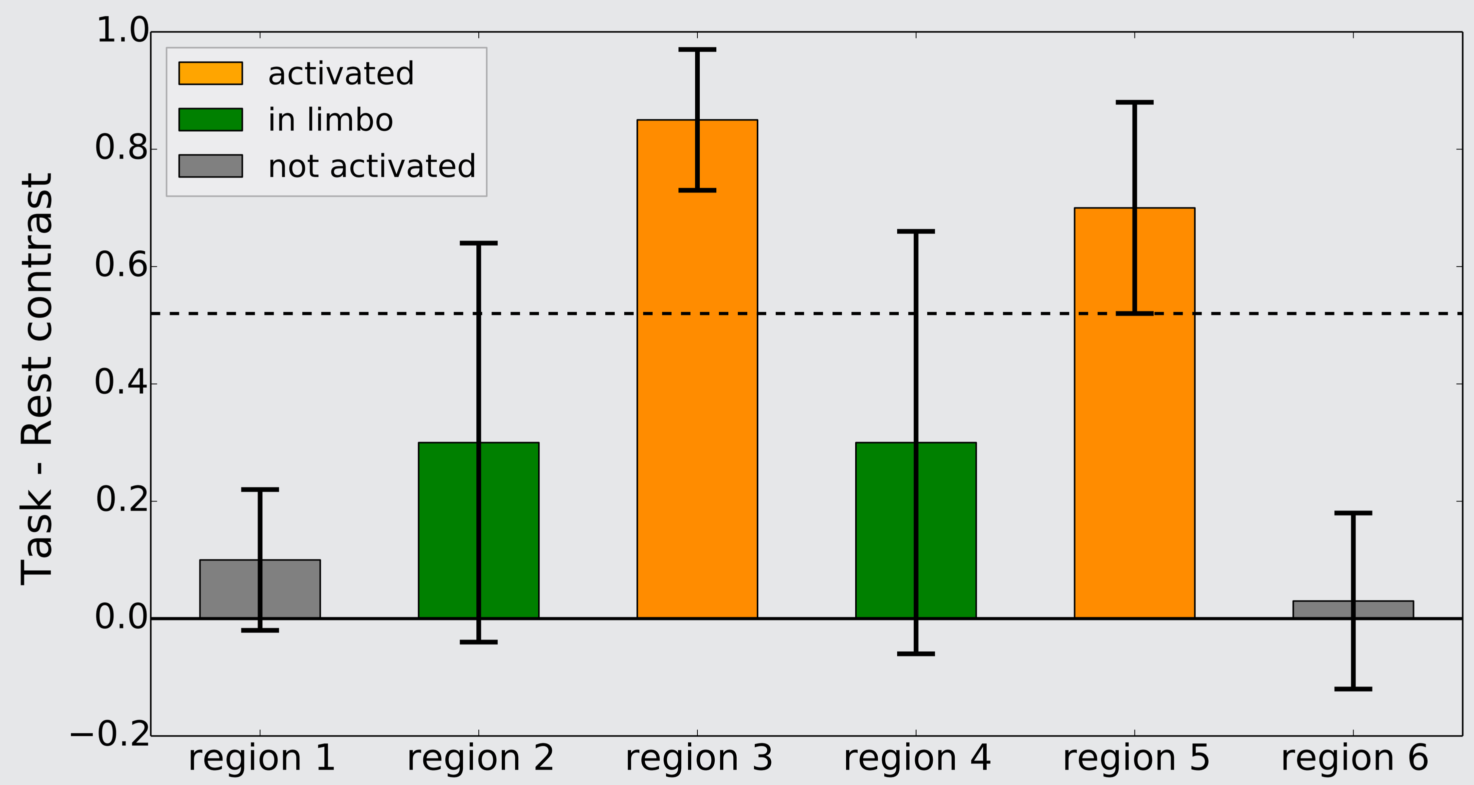
   In the case of a **level 1 analysis**, for every non-significantly activated voxel, a t-value and significance level is calculated for the difference between this voxel and the comparison voxel:

$$t_{\text{in limbo}} = \frac{c\beta_i - c\beta_v}{cV_i c' + cV_v c' - 2cV_{iv}c'},$$

   where c is the contrast of interest, β_i the parameter estimate and V_i the variance in the n.s. voxel, and β_v and V_v the parameter estimate and variance matrix in the comparison voxel. V_{iv} is the covariance between these two voxels.

   In the case of a **level 2 analysis**, a weighted least squares (WLS) GLM is used. The weights are set to the inverse of the individual variances of the difference between the n.s. and comparison voxel of each subject.

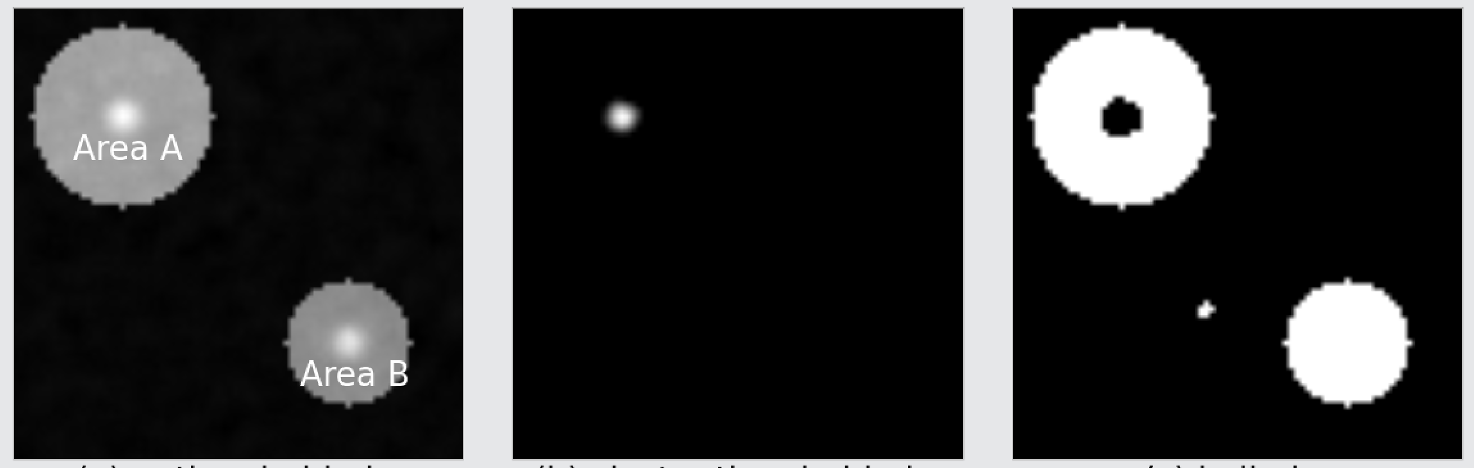
Example In Limbo Approach



Simulation Studies

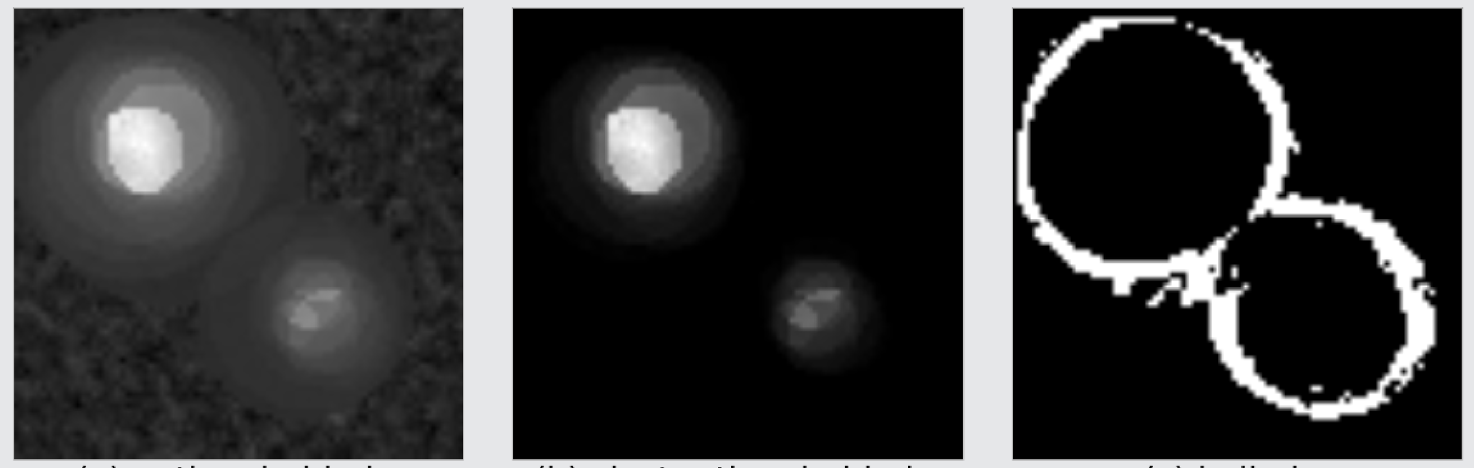
The approach was applied to simulated data (using neuRosim (Welvaert et al., 2012), both in a level 1 and a level 2 analysis.

Level 1 analysis



(a) unthresholded z (b) cluster-thresholded z (c) in limbo

Level 2 analysis

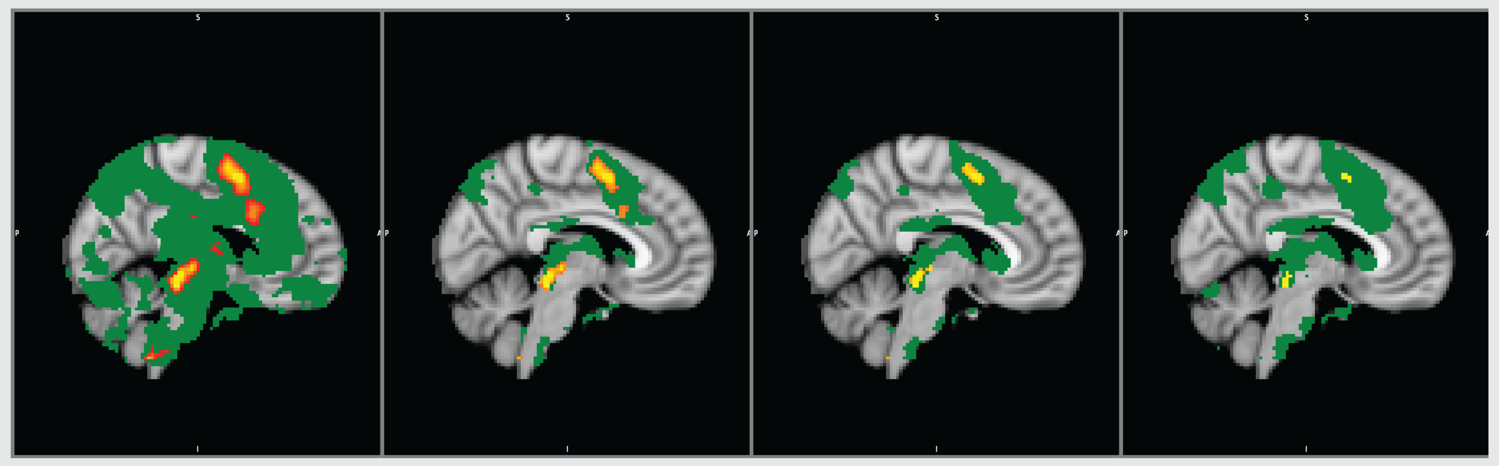


(a) unthresholded z (b) cluster-thresholded z (c) in limbo

Application to Real fMRI Data

The approach was also applied to real fMRI-data from a study on the neural basis of the speed-accuracy tradeoff by Forstmann et al. (2008), showing its feasibility and the rather large amount of in limbo areas when using lower z-thresholds.

z=2.3 z=3.1 z=3.7 z=4.1



References

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