14.03.2019

OCD Network Status

# Data Transformation

The BOLD data were transformed into three representations of functional connectivity: the demeaned, detrended BOLD signal; the z-scored BOLD signal; and the BOLD signal phase.

# Assembly Detection

The fastICA algorithm of Aapo Hyvärinen was used to search for assemblies in each data representation. Assemblies were computed on the entire time series of each representation in order to ensure comparability between control and patient assemblies, with the number of independent components detected using principal component analysis

For the 90-region parcellation, the filtered BOLD signal displayed 15 independent components, the z-scored signal displayed 15 independent components, and the Hilbert-phase signal displayed 16 independent components. The 116-region parcellation displays 17 independent components in the BOLD signal, 18 independent components in the z-scored signal, and 20 independent components in the Hilbert-phase signal.

# Significantly Differing Assemblies: OCD vs. Controls

Following the detection process, the activation time course of each assembly was split into the obsessive-compulsive dataset and the control dataset. The control time courses were then compared to those of obsessive-compulsive patients using the Kolmogorov-Smirnov two-tailed test in order to determine which assemblies displayed significantly different activation distributions between conditions. The number of these assemblies is listed as a second column in the index of number of assemblies.

For the 90-region parcellation, only the Hilbert-phase representation displays significantly different activation distributions between OCD and control subjects. This representation possesses 13 assemblies with significantly different activation distributions between conditions. The 116-region parcellation shows one assembly with significantly different activation profiles in the narrowband BOLD signal, none in the z-scored representation, and 11 in the Hilbert-phase representation. It must be observed, however, that the number of significant assemblies varies from run to run.

**90 Regions**

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**116 Regions**

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# Comparing Assemblies Directly

In this section, we calculate the correlation in ROI weights and in assembly activation profiles between assemblies. We restrict our analysis to those assemblies displaying significantly different activation profiles between conditions.

## 90-Region Parcellation:

### Membership: inter-assembly membership correlation coefficients ranged between -0.2 and 0.2, with most assembly correlation remaining between 0 and 0.1. This suggests that assemblies generally share a small proportion of elements, but this overlap tends to be small. However, this correlation is run on the weighted membership vectors rather than on binarized membership vectors, which may create a misleading impression of shared membership. The analysis should be repeated with binarized membership vectors in order to more precisely determine the inter-assembly proportions of shared regions.

### Activation: virtually no correlation was found in the activation time series of different assemblies. This is to be expected, as the independent component algorithm maximizes the inter-component activation independence.

## 116-Region Parcellation:

### **90 Regions**

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### **116 Regions**

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# Comparing Assemblies between Conditions

In this section, we calculate the correlation in in assembly activation profiles between the same assemblies in different conditions. Once again, we restrict our analysis to those assemblies displaying significantly different activation profiles between conditions.

## 90-Region Parcellation:

### Assemblies displayed very limited activation correlation between conditions. Cross-condition correlation generally ranges in magnitude from *O(10-3)* to *0.05*. This finding somewhat surprises me, as I would expect activation patterns to display some similarity between conditions.

#### It must be born in mind that different conditions also reflect different subjects, so inter-subject variation will affect the correlations.

#### It may also be that correlation is a poor measure for activation distribution similarity. As such, using an alternative metric, e.g. the Kullback-Leibler divergence, may better capture similarity and differences in activation distributions.

## 116-Region Parcellation:

# Assembly Connectivity Maps

In this section, we calculate the connectivity maps of the assemblies displaying significantly different activation profiles between conditions. These maps are calculated as the outer product of each assembly’s membership vector and are displayed as both weighted adjacency matrices and cortical network maps. Additionally, the membership weight vectors are displayed.

## 90-Region Parcellation:

### The formatting of the cortical maps and assembly matrices appears to be flawed. I am not certain why, as previous runs did not display this problem. It may be due to the unusually high number of significant assemblies on this run (13 significant assemblies, as compared to the more standard eight).

## 116-Region Parcellation:

## **90 Regions**

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# Future Steps

Now that we have established that there exist assemblies with significantly different activation distributions between OCD and healthy patients, what remains is to compile the most interesting results, to determine which current analyses may be misleading or superfluous, to select alternative analyses which may further strengthen the current results, and to formulate questions and stages for future analyses. Here, we attempt to run through these stages.

## Interesting Results

## Misleading or Superfluous Analyses

### Correlation analyses between conditions may be flawed due to confounding factors, e.g. inter-subject variation.

### Display of the significance of the difference in total activation distributions between conditions is labeled *entropy* rather than *activation*. This should be corrected and the analysis expanded to include the activation distribution type per condition, per assembly, and per subject.

### The original assembly labels are not retained during the process of detecting significant assemblies. This can lead to some confusion as to which assemblies display significant activation differences between conditions.

### Assembly membership correlation is intended to detect proportion of shared regions between assemblies. Use of weighted membership vector likely confuses this analysis; should be binarized.

### Assembly connectivity matrices are poorly displayed.

## Additional Analyses

### Repeat correlation analyses

#### On subjectwise basis: examine effect of subject-by-subject variation

#### With KL divergence in order to confirm results

### Quantify difference in information content / flexibility (entropy) between conditions, both in total and on a per-assembly basis.

## Questions for Future

### Which condition possesses greater flexibility / contains more information?

### What type of distribution do the activation and entropy distributions follow

#### Per condition?

#### Per assembly?

#### Per subject?

### How distinct are the activation and entropy distributions

#### Between conditions?

#### Between assemblies?

#### Between subjects?

### Which effective connectivity features significantly differ between conditions?

### How do assembly activation and transition probabilities differ between conditions?

### If ICA is run on OCD and healthy data *separately*, do the OCD assemblies significantly differ in membership from the healthy assemblies?

### Can one demonstrate similarity between OCD assembly characteristics and those of other compulsive disorders, e.g. addictive or eating disorders?

#### Quantify similarity between assembly memberships and activation distributions per condition

## Future Analyses

### Plot entropy for each condition:

#### Total (sum)

#### Assembly-wise

### Plot activation distribution:

#### Total per condition

#### Per condition for each significant assembly

#### Per subject for each significant assembly

### Run [KL divergence](https://en.wikipedia.org/wiki/Kullback%E2%80%93Leibler_divergence) on activation distributions:

#### Total distribution, divided between conditions

#### Assembly-wise distributions, divided between conditions

#### Assembly-wise distributions, divided between subjects

### Search effective connectivity:

#### Confirm symmetry of FC, SC data

#### For each subject, calculate effective connectivity using mean value of all assemblies

#### Search for differences between subjects/conditions in each assembly using the [Network Based Statistic](https://sites.google.com/site/bctnet/comparison/nbs).

### Project assemblies into PMS space:

#### Quantify activation and transition probabilities for each assembly

#### Define two PMS spaces: “healthy” PMS space vs. “compulsive” PMS space