Mean conditional probability of recurrence as a method for detecting coupling
directions between brain areas and identifying central hubs of fMRI resting state
effective connectivity

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**Background:** Network topological analysis of fMRI resting state based on adjacency matrices is a popular method for obtaining information about the interrelationship between brain areas and for identifying hubs of brain connectivity. A widely used method to create adjacency matrices is the calculation of Pearson’s correlation coefficient, but its linear and symmetric properties make it unsuitable to detect nonlinear relationships and effective connectivity. This results in undirected graphs and thus neglects information about whether a hub distributes or integrates information. Moreover, finding an optimal threshold criterion for obtaining adjacency matrices remains a controversial issue and measures of network topology are highly dependent on the thresholded adjacency matrix.

**Methods:** Resting state data of 93 subjects (mean age: 25.5, SD: 5.0) were analyzed and phase space reconstruction of the preprocessed data was performed in order to create recurrence plot matrices, a two-dimensional representation of the recurrences of trajectories to a neighborhood in high-dimensional phase space of a dynamical system. Directed and weighted graphs for a set of 112 regions based on the Harvard-Oxford atlas were obtained by calculation of mean conditional probability of recurrence. Mean conditional probability of recurrence is a measure that utilizes recurrence plots to identify the coupling direction between two dynamical systems. In order to obtain thresholded adjacency matrices, significance of coupling was established by creating twin surrogate data, i.e. trajectories from the same system but starting at different initial conditions. In order to identify central hubs of effective connectivity, indegree centrality, outdegree centrality and overall degree centrality (indegree+outdegree) was calculated for every subject and averaged over subjects for further group analysis.

**Results:** The highest values for overall degree centrality were found for left and right planum temporale, lingual gyrus, insular cortex and precentral gyrus. The highest values of indegree centrality were found for left and right planum temporale and lingual gyrus and the highest values of outdegree centrality were found for left and right insular cortex and precentral cortex. These results point towards the role of these brain areas as central hubs of information integration and information distribution in resting state brain effective connectivity. Moreover, it was found that significant connections between brain areas obtained by mean conditional probability corresponded in part to small and non-significant Person correlation coefficients in the range of -0.2 to 0.2, pointing towards its inadequacy in capturing important dependencies between brain areas, when using significance of correlation as threshold criterion.

**Conclusions:** Directed graphs obtained via mean conditional probability of recurrence offer a way to detect significant linear and nonlinear coupling directions between brain areas in fMRI resting state data. Adjacency matrices based on significant Pearson correlation coefficients might miss important connections between brain areas and could lead to biased measures of network topology.