A Functional Geometry of fMRI BOLD Signal Interactions

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1 Objective

We propose a method that captures the global patterns of functional connectivity [1] in the brain from a set of *blood oxygenation level dependent (BOLD)* signals in *functional magnetic resonance imaging (fMRI)* data acquired during a certain condition or task. The method represents the connectivity as a *diffusion process* on all points in the brain. By embedding the corresponding BOLD signals, into a *diffusion map*, or a so-called *functional geometry* we capture all pairwise relations of the signal in a Euclidean geometry. In this geometry proximity signifies close functional connectivity. The embedding captures relations on multiple scales, which are parameterized by the diffusion time. It establishes a space, wherein the roles of individual brain regions, their interaction with others, and the change and dynamics due to different conditions can be studied. The approach provides an explorative tool for the analysis of global interaction patterns in the brain, their correspondence with specific tasks, and their descriptiveness with regard to clinically relevant questions.

The work is in the same vein as [2] where diffusion maps were used to perform dimensionality reduction by parameterizing entire brain states, to represent relations between brains. In Shen et al. [3] they were used to segment activated regions. In [4] initial density measurements of pre-chosen regions in functional geometries were related to certain tasks. In this work we present complete results of a method that detects regions of interest and measures their mutual relations, and relates them to clinically relevant variables. In the following we outline the method, present results, that indicate that the functional geometry is able to repeatably capture differences between subject sets. We conclude with a discussion of the method and its relation to existing approaches.

2 A Diffusion Distance between BOLD Signals

The method first establishes pair-wise relations between all BOLD signals in the brain. Based on this set of mutual relations a Markov chain and a corresponding diffusion map [5] are built. We derive the map from a set of signals $\{\mathbf{x}_1, \ldots, \mathbf{x}_m\}$, where $\mathbf{x}_i \in \mathbb{R}^n$. Each signal is represented by a node i in a graph, which are mapped to a manifold $\{\mathbf{\Psi}_i, \ldots, \mathbf{\Psi}_m\}$ in the *functional geometry*. In our case, each $\mathbf{x}_i$ is the BOLD signal observed at one position in the brain for n time points. An affinity kernel $k_{ij} = corr(\mathbf{x}_i, \mathbf{x}_j)$ is transformed to the transition probabilities of a Markov chain, by normalizing with the degree of each node $p_{ij} = k_{ij}/d(i)$. The Markov chain on the set of nodes defines a diffusion process and a corresponding family of *diffusion distances* on the set of nodes: $D_t(i,j) = \sum_{l=1,\ldots,m} \frac{(p_t(i,l)-p_t(j,l))^2}{\pi(l)}$ where $\pi(i) = \frac{d(i)}{\sum_j d(j)}$. They correspond to the diffusion operator P, and its powers P^t where t is the diffusion time and define a family of geometries on the set of nodes that reflects the structure of their mutual connectivities. The distance D_t is low if there is a large number of paths of at most length t with high transition probabilities between the nodes i and j. The nodes can be mapped to a Euclidean geometry by an eigenvalue decomposition of P. It results in a sequence of eigen values $\lambda_1, \lambda_2 \ldots$ and corresponding eigen functions $\Psi_1, \Psi_2, \ldots$ that fullfill $P\Psi_i = \lambda_i \Psi_i$. In this space $\|\mathbf{\Psi}_t(i) - \mathbf{\Psi}_t(j)\| = D_t(i,j)$. Thereby the *functional* relations between fMRI signals are translated into spatial distances in the functional geometry.

To use the geometry for the analysis of functional networks we compare the maps of groups of individuals. Before comparison, maps are aligned by a Procrustes analysis to exclude effects of rotation and translation that do not correspond to actual changes in the local geometry. After alignment, the nodes of a set of subjects

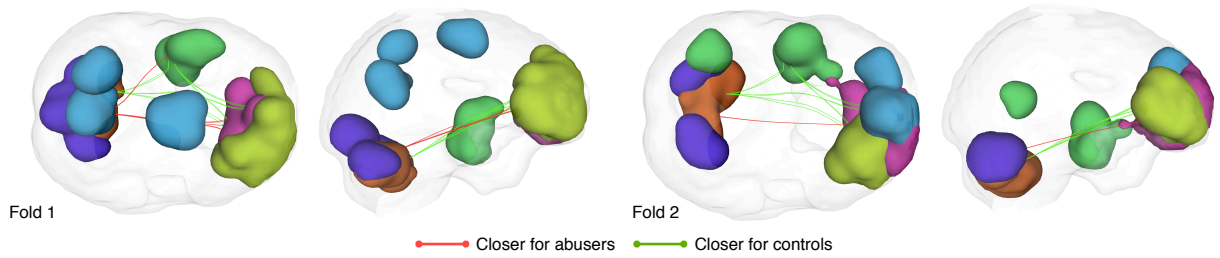

Figure 1: Results from experiments on two disjoint groups of subjects: Each fold consists of 12 individuals, of which 6 are cocaine abusers, and 6 are healthy control subjects. For each set, first the points in the functional geometry with the largest displacement between abuser and control group were chosen. They were clustered according to their position in the functional geometry, and the displacement vector between control and abuser. Finally for each groub the mutual distances between the clusters are measured, and those with a significant difference in distance between controls and abusers are marked as red/green lines in the figure. Red indicates closer for abusers, while green indicates closer for controls. Note the very consistent measurements across the two evaluation sets of subjects.

are mapped to distributions in the functional geometry. We can compare both the position and the mutual distances between clusters that behave in a coherent manner.

3 Results

We built maps from a set of 24 subject (12 cocaine abusers, 12 healthy controls). The subjects performed a reward processing task during which they were told in advance the amount of money they would be given if the performed a basic Go/NoGo task correctly. Cocaine abusers were hypothesized to have different sensitivity to reward than control subjects. A detailed description is given in [4]. To evaluate the functional geometry we build maps from two randomly chosen distinct sub-sets, each containing 12 subjects (6 abusers/6 controls). For each of those folds the nodes with a significant position difference are selected and clustered according to their position and position difference between abusers and controls. The mutual functional geometry distances between the resulting clusters are then measured. For both evaluation folds the connections with significant differences between the two groups (abuser/control) were compared. Fig. 1 shows the resulting clusters, and connections for both sets. For both sets 6 clusters were identified. The correspondences of clusters across the two sets were established only for visualization purposes based on their centroid position.

4 Discussion

We view the interaction processes in the brain as a diffusion process, based on the mutual correlation of BOLD signals. The resulting family of diffusion maps allows for the integration of hierarchical connections between different regions. The embedding captures the global functional connectivity structure of the brain, and can detect differences between clinical populations. It is useful for the exploratory analysis of fMRI data, the formulation and quantification of hypotheses regarding regions and the change of their functional relation to other areas. Ongoing work is focusing on the robust detection of those differences despite the difficulty of describing them with simple models, and their usability for the localization of functional networks.

References

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