An Optimized Clustering Technique for Functional Parcellation of Hippocampus

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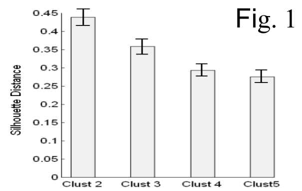
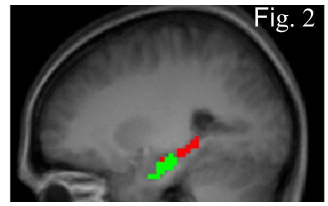
Introduction

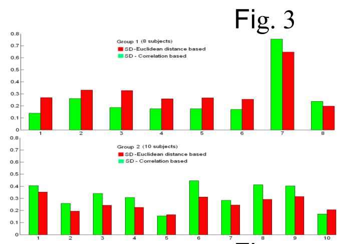
Functional sub-division of important anatomic regions in the human brain is normally based on anomaly in structural connectivity patterns [1] or functional connectivity maps, after subdividing the region of interest on trial basis [2]. Quantification of functional heterogeneity, and determining number of sub-regions on the basis of that, has rarely been a focus of study. This work is centered around implementation of self organized maps (SOM) to classify the functionally different regions in the hippocampus as it exhibits functional and anatomical differences in patients with disorders such as schizophrenia, bipolar disorder, and depression [3]-[5]. We rigorously tested the performance of SOM with conventional k-mean clustering techniques to optimize how many heterogeneous compartments the left hippocampus possesses on the basis of connectivity maps associated with each voxel in the ROI. We designed and used an in house software with SPM5 to parcellate functionally heterogeneous ROIs using SOM.

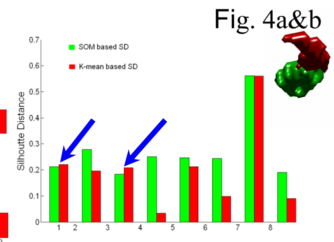
Method

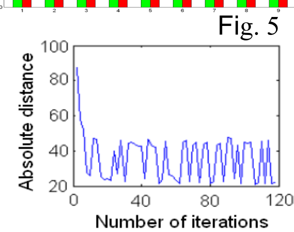
Resting state 3T fMRI data from 18 volunteers was processed to remove movement-related and global signals, then low-pass filtered at 0.1 Hz. A left hippocampus region of interest (ROI) was defined using the Harvard-Oxford atlas for 8 subjects (group 1) and remaining 10 (group 2) ROIs were outlined manually. Functional connectivity maps were calculated for each hippocampus voxel by regression of each brain voxel's time series on the hippocampus voxel's time series. We then segmented the ROI into sub-regions using self-organized mapping (SOM). SOM is a supervised learning algorithm that learns to detect regularities and correlations in its input vectors and adopt future responses to that input accordingly. A test on subjects with common ROI (group 1) was conducted to determine the optimal number of clusters by measuring the *silhouette distance* (SD) [6] as we vary the number of groups (*Fig 1*). Based on inter-subject overlap criteria we determined two sub-regions to be optimal for the clustering analysis. In a separate test we measured the SD using k-mean clustering for the first group and the measured value of SD is found to more for SOM based clustering (Fig. 4a) except two subjects where k-mean performed marginally better (blue arrow). The inputs to the SOM were the connectivity maps associated with each voxels in the hippocampus. We performed the analysis for the first group in the common ROI, producing connectivity maps for each hippocampus cluster. A group summary of the resulting hippocampus subdivision was generated by assigning voxels to each cluster when at least 5 subjects contained that voxel in each group. Individual roi based analysis was then performed on 10 subjects and the *silhouette distance* was measured based both on Euclidean distance and PPM correlation measured within and out side the group.











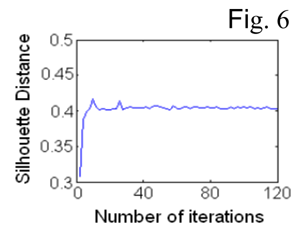


Fig 1. Measured value of SD vs number of clusters in the analysis. Fig. 2. Segmented left hippocampus (saggital view on MNI template).Fig. 3. Comparison of SD calculated based on Eucleadian distance and correlation in group space(top) and individual space (bottom). Fig 4a Comparison of clustering efficiency between k-mean and SOM technique in the group space. Fig 4b. Anterior and Posterior part of segmented hippocampus in the group space. Fig. 5 Number of iteration vs absolute distance between successive neuron weights. Fig. 6. SD vs iterations for SOM.

Results

All the subjects exhibited distinct clusters along the long axis of the hippocampal structure; Figure 2 shows the group voxel assignments, indicating a clear anterior/posterior functional division of the hippocampus. Anterior and posterior portions of the hippocampus in case of common ROI exhibited distinct patterns of functional connectivity with anterior and posterior cingulate cortex ($p<0.005$). However, the parcellation of anterior and posterior part of left hippocampus in the individual space is more consistent and robust as the correlation based SD is more than Eulidean distance based SD except for one subject, which shown clearly an opposite trend in the other group (Fig. 3). Figure 5 shows variation of absolute distance between the current and preceding neuron weights associated with a particular cluster. Figure 6 shows the variation of SD as the SOM progresses. A comparison of performance with k-mean clustering in terms of the SD clearly favors the use of SOM in this analysis (Fig. 4a).

Conclusions

We were able to delineate sub-regions of hippocampus distinguishable by their different patterns of functional connectivity with the neocortex. The self-organized mapping procedure offers a data-driven and automated method, which requires numbers of sub-regions to be determined either based on SD value or prior knowledge. However, optimization of functional subdivision based on clustering efficiency measure such as SD is essential to accurately determine the functional heterogeneity.

References

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