Automated Segmentation of the Human Amygdala using High Angular Diffusion Imaging (HARDI) and Spectral k-means Clustering

Brian David Stirling[1], Yu-Chien Wu[1], Long Sha[1,2], Jim Haxby[1], and Paul J Whalen[1]

[1]*Psychological and Brain Sciences, Dartmouth College, Hanover, NH, United States,* [2]*Neuroscience Institute, New York University, New York, NY, United States*

Target Audience: Neuroscientists, Psychologists, Psychiatrists, MRI scientists interested in diffusion imaging, Clinicians whose research focuses on amygdala.

Introduction: The amygdala, a subcortical structure in the human brain associated with fear and emotion, appears as a small region of grey matter using conventional T1W imaging despite a number of functionally distinct subnuclei that connect with different regions of the brain. Having an accessible approach for imaging these subnuclei would be of great value for furthering the understanding of the amygdala. Two experiments have been able to segment the amygdala into four distinct regions, one with manual segmentation using ultra-high resolution T1W imaging[1] and another using diffusion tensor imaging (DTI) with probabilistic tractography[2]. Both experiments, however, used *a priori* knowledge for segmentation. To increase accessibility and efficiency, it may be helpful to use a data-driven approach. Two other experiments used k-means clustering, an automated machine unsupervised learning technique, on the diffusion tensor to segment the amygdala into a medial and lateral region[3] as well as a deep and superficial region that corresponded to anatomical connectivity[4]. The present study uses High Angular Resolution Diffusion Imaging (HARDI), which accounts for crossing fibers, as well as high spatial resolution with a voxel size of 1.6x1.6x1.6 mm^3. Spectral k-means clustering was used on the spherical harmonic (SH) coefficients calculated from orientation distribution functions (ODF) of each amygdala voxel. We hypothesized that, compared to conventional DTI approaches, these imaging methods would allow for segmenting finer structures of the amygdala.

Methods:

MRI Acquisition: High spatial resolution HARDI was performed on 32 healthy volunteers at a 3.0T Philips Achieva INTERA scanner with a 32-channel head coil. The DW pulse sequence was SS-SE-EPI. MR imaging parameters: FOV=230mm, matrix size=144x144, voxel size=1.6x1.6mm, 22 slices with thickness=1.6mm, TE/TR=79/3382ms, 4 repetitions. DW parameters: δ/Δ=21/39ms, one b-value=0s/mm^2 and 61 noncollinear DW directions at b-value=1000 s/mm^2. Other imaging protocols included a T1W image, a fieldmap sequence and whole brain coverage HARDI with cubic voxel size of 2x2x2mm^3.

Data processing: Each volume of the DW images of the high spatial HARDI were motion-, eddy current-, and fieldmap-corrected before being averaged over the four repetitions. In the diffusion space, the structural ODF profiles of the amygdala were computed using in-house MATLAB programs with Q-ball Imaging (QBI)[6] algorithms on the averaged HARDI data. SH coefficients of each ODF profile were extracted up to an order of 6, i.e., l_{max}=6. Only coefficients of even orders (total 28 SH coefficients) were entered into the subsequent spectral clustering. The amygdala probability mask was first obtained from the Harvard-Oxford subcortical structural Atlas in the MNI152 standard space and then warped to the subject diffusion space using FSL-FNIRT nonlinear registration.

Spectral clustering: The similarity matrix, S, was computed using the following algorithm $S_{ij} = \exp\left(-sin^2\left(\frac{cos^{-1}(C_{ij})}{2}\right)/sigma^2\right)$, where C is the distance matrix of the SH coefficients across voxels within the amygdala. The distance matrix was based on pair-wise Pearson's correlation coefficient, weighted by the corresponding voxel mutual euclidean distance. We then transformed the similarity matrix into normalized symmetric laplacian matrix, and performed eigendecomposition on the laplacian matrix. Next, we created a null distribution of eigenvalues of the laplacian matrix by randomizing the SH coefficients (bootstrapping 1200 iterations). Eigenvalues of the Laplacian matrix based on data were tested against the null distribution using zscoring. We determined the number of significant eigenvalues to be the number of clusters, denoted as N. The k-means clustering with correlation distance was then applied on the first N eigenvectors. Lastly, clusters were averaged across subjects (n=32) and checked for consistency.

Results: In this study, consistantly three eigenvalues of the Laplacian transformed similarity matrix were found to be statistically significant across 32 subjects with $p < .001$. Therefore, three was the optimal cluster number for this study and included the following regions: medial (red), posterior-superior-lateral (green), anterior-inferior-lateral (blue). The ODF profiles of the right amygdala with various orientations, shapes, and peaks are shown in Fig. 1. The ODFs were overlaid on the results of the clustering algorithm from one subject on an axial slice. Fig. 2 shows the similarity matrix of the SH coefficients of the ODF profiles for the left amygdala. A 3D scatter plot of the center of masses of each cluster across subjects for the left amygdala is shown in Fig 3. Fig. 4 shows the consistency map of clusters across subjects overlaid on axial, coronal, and saggital T1W slices for the left amygdala, clearly showing three clusters.

Discussion and Conclusions: This study showed that with higher angular resolution diffusion imaging and higher spatial imaging resolution we are able to segment amygdala into three clusters. The automated clustering used only structural information within the amygdala and did not require prior knowledge of amygdaloid structure[1] and of cortical functional projections of amygdaloid subnuclei[2]. Further study will incorporate probabilistic tractography to link each cluster to functionally relevant cortical regions as well as high resolution T1W and Susceptability Weighted Imaging (SWI) to identify the subnuclei within each cluster.

References: 1. Entis et al., NeuroImage 2012; 60(2):1226-1235. 2. Saygin et al., NeuroImage 2011; 56(3):1353-1361. 3. Solano-Castiella et al., NeuroImage 2010; 49(4):2958-2965. 4. Bach et al., J Neurosci 2011; 31(2):618-623. 5. Luxburg, Stat Comput 2007; 17(4):395-416. 6. Tuch, MRM 2004; 52(6):1358-1372.

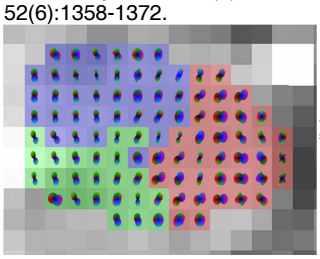

Fig. 1: Right amygdala (axial) with ODF overlaid on T1W for one subject.

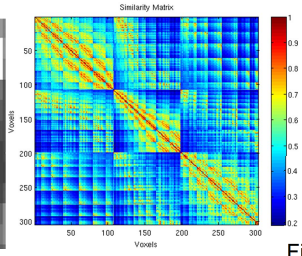

Fig. 2: Left amygdala similarity matrix for k=3. Three distinct regions are noticeable. Red suggests high similarity.

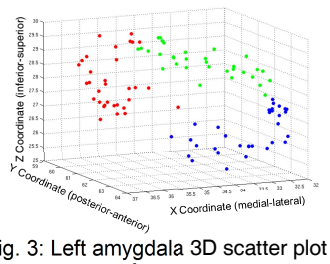

Fig. 3: Left amygdala 3D scatter plot of cluster center of masses across subjects. Coordinates are by voxels. Oriented to match with coronal view in Fig. 4

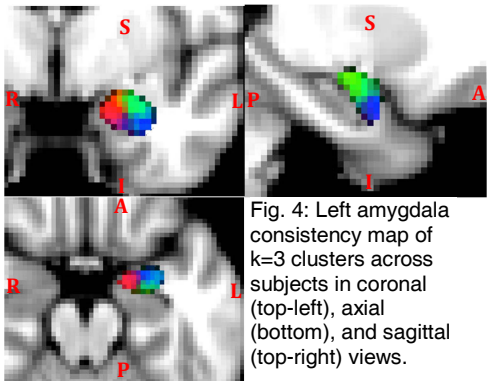

Fig. 4: Left amygdala consistency map of k=3 clusters across subjects in coronal (top-left), axial (bottom), and sagittal (top-right) views.