Tensor-based morphometry and classifier algorithms for the identification of structural brain changes in geriatric depression

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Introduction

Depression in the elderly is common and causes significant morbidity and mortality. Most experts believe that the biological changes in geriatric depression have multiple causes, including neurodegeneration (particularly prodromal Alzheimer's disease), cerebrovascular changes, and stress-induced neurotoxicity from chronic illness. Consistent with this "heterogeneity" model, previous studies in geriatric depression have reported multiple, and sometimes conflicting, findings, including decreased volumes in the prefrontal cortex, the medial temporal lobe, and the striatum. Recently, several research groups have developed multivariate methods for the analyses of structural brain images using classifier algorithms. These approaches are designed to identify brain changes that are "spatially complex and subtle…(and) due to a variety of factors" [1], and thus seem particularly well-suited for the study of geriatric depression. In this study, we adapt and extend methods used in [2], to identify the volumetric brain changes associated with geriatric depression.

Methods

Subjects: Data from 26 subjects were analyzed. These included 13 elderly control subjects, 6 male, mean age = 68.7, SD = 6.0, and 13 elderly subjects with major depressive disorder, currently in a major depressive episode (mean Hamilton Rating Scale for Depression = 18.5, SD = 4.8), 5 male, mean age = 71.3, SD = 6.3. Other than Major Depressive Disorder (for subjects in the depressed group) and the anxiety disorders, all other Axis I psychiatric disorders were used as exclusion criteria. Subjects were also excluded for a prior history of stroke or significant head injury, Alzheimer's, Parkinson's, or Huntington's disease. All depressed subjects had late-onset geriatric depression, with their first episode of depression starting after the age of 50 (mean age of depression onset = 67.6, SD = 7.2). All subjects were right-handed.

Imaging Methods: Subjects were scanned using a 1.5 Tesla Signa Scanner (GE Medical Systems, Milwaukee, WI). 3D structural MR images were acquired at sagittal orientation using 3D SPGR (TR/TE = 5/25 ms; flip angle = 40º; FOV = 24X18cm, slice thickness = 1.5mm, matrix = 256x192).

Computational Methods: As in [2], we used a tensor-based method for generating a large number of voxel-wise features for each subject. Each of the subject images was registered to an atlas (MNI-Colin) with a local, nonlinear, deformable transformation to produce a deformation field. The registration was implemented using the Finite Element Method in the Insight Segmentation and Registration Toolkit [3]. Statistical maps were produced that capture local shape differences between each subject and the atlas by computing a Jacobian matrix at each element in the deformation field. The Jacobian matrices were then converted into tensor maps by the taking the Jacobian determinant. The determinant of a given Jacobian matrix reflects the contraction or expansion of that image's region relative to the template; values less than 1 reflect contraction while values greater than 1 reflect expansion. To reduce the number of image features in each subject's tensor map, the maps were down-sampled by a factor of 4 to obtain 30,983 features. We next applied feature selection to identify the fewest number of features (4.0 x 4.0 x 4.0 mm voxels of the brain) that could effectively distinguish between geriatric depressed patients and controls. Feature selection was done using a recursive feature elimination (RFE) algorithm in the Gist Machine Learning Tools [4] with leave-one-out (LOO) cross validation to test the validity of the classification. RFE trains a linear support vector machine (SVM) and removes 50% of the features with the lowest weights. This process is iterated until the least number of features with the best classification accuracy is determined. The selected features were then used in an SVM to test the overall "separation" and "prediction" of the dataset. Prediction accuracy was evaluated by testing the SVM on subjects excluded from both feature selection and SVM training (i.e., subjects not previously seen by the algorithm). Separation accuracy was evaluated by testing on subjects excluded from training (but included during feature selection).

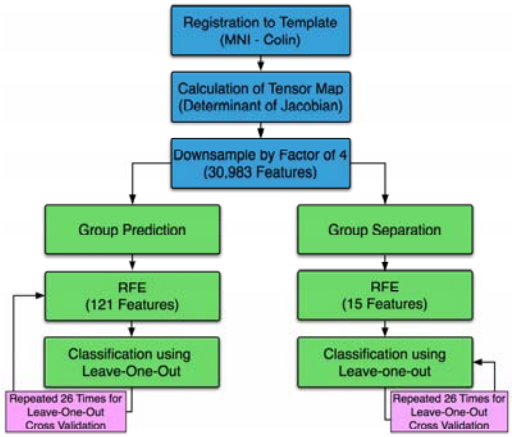

Figure 1: Flowchart showing methods that constitute methods for feature selection and classification.

Results

Group Prediction: Applying RFE and SVM algorithms with a linear kernel resulted in 65.48% classification accuracy using LOO cross validation. Each of the 26 subjects had 121 features identified. The intersection of these features from each of the 26 subject resulted in 18 key features as shown in Figure 2. Training a linear SVM with the 18 features provided a 100% classification accuracy using LOO cross validation. The features identified included the prefrontal cortex and the striatum, as found in previous volumetric studies of geriatric depression.

Group Separation: Testing for separation using LOO cross validation with a linear SVM led to 92.31% with 15 features. The features were similar to those identified in the "prediction" test above.

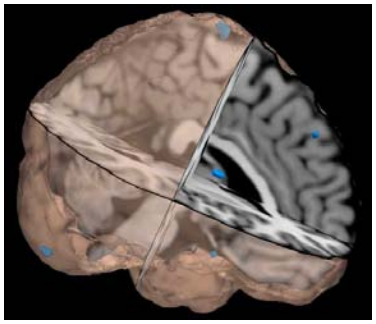

Figure 2: Key features identified with feature selection included the prefrontal cortex and the striatum.

Conclusion

The features obtained included prefrontal and striatal regions of the brain. All selected features had negative values relative to the control subjects, reflecting a relative volumetric contraction. This preliminary study shows that SVM and tensor-based morphometry methods can be used to classify individuals with complex neuropsychiatric disorders, such as geriatric depression. In future studies we plan to use these methods to identify subgroups of geriatric depression, and ultimately inform treatment decisions.

References

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[3] Insight Segmentation and Registration Toolkit (www.itk.org)

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