Challenges of Trustable AI and Added-Value on Health
B. Séroussi et al. (Eds.)

doi:10.3233/SHTI220395

Automated Diagnosis of Autism Spectrum Disorder Condition Using Shape Based Features Extracted from Brainstem

Vaibhav JAIN[a], Abirami SELVARAJ[a], Rakshit MITTAL[b], Priya RANI[c], Anandh KILPATTU RAMANIHARAN[d] and Jac Fredo AGASTINOSE RONICKOM[a]
[a] *School of Biomedical Engineering, Indian Institute of Technology (BHU), India*
[b] *Telecom Paris, Institut Polytechnique de Paris, Palaiseau 91120, France*
[c] *Applied Artificial Intelligence Institute, Deakin University, Victoria, Australia*
[d] *The University of Alabama at Birmingham, United States of America*

Abstract Alterations to the brainstem can hamper cognitive functioning, including audiovisual and behavioral disintegration, leading to individuals with Autism Spectrum Disorder (ASD) face challenges in social interaction. In this study, a process pipeline for the diagnosis of ASD has been proposed, based on geometrical and Zernike moments features, extracted from the brainstem of ASD subjects. The subjects considered for this study are obtained from publicly available data base ABIDE (300 ASD and 300 typically developing (TD)). Distance regularized level set (DRLSE) method has been used to segment the brainstem region from the midsagittal view of MRI data. Similarity measures were used to validate the segmented images against the ground truth images. Geometrical and Zernike moments features were extracted from the segmented images. The significant features were used to train Support vector machine (SVM) classifier to perform classification between ASD and TD subjects. The similarity results show high matching between DRLSE segmented brainstem and ground truth with high similarity index scores of Pearson Heron-II (PH II) = 0.9740 and Sokal and Sneath-II (SS II) = 0.9727. The SVM classifier achieved 70.53% accuracy to classify ASD and TD subjects. Thus, the process pipeline proposed in this study is able to achieve good accuracy in the classification of ASD subjects.

Keywords Autism spectrum disorder, Brainstem, Level set method, Geometrical features, Zernike moment, Support Vector Machine

1. Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental condition characterized by significant challenges in social interaction, communication, and repetitive patterns of behavior which are mainly controlled by brainstem [1]. Anatomical differences in the brainstem region have been identified as an essential biomarker for ASD [2]. Due to its time consuming nature, along with absence of any notable discriminator, the diagnosis of ASD is often delayed [3]. This necessitates the need for a reliable diagnostic technique for ASD. Structural Magnetic Resonance Imaging (sMRI) is one of the most commonly used imaging modality that offers non-invasive methods to screen anatomical anomalies related to neuronal activation. Segmentation of the region of interest is a daunting task and due to the complexity and resource-intensive nature of manual segmentation, the brainstem is segmented using automated techniques, such as level set methods. Level set algorithms are known to develop irregularities which are generally treated with re-initialization, that stabilizes the level set evolution, however leads to numerical inaccuracies [4]. To avoid the re-initialization problem, distance regularized level set methods (DRLSE) are deployed which use an external energy component and distance regularization term, to force the zero level contours to the prescribed location and maintain its shape [5]. Geometrical [6] and tensor based [7] features are used to infer the shape, size, orientation of brainstem in ASD patients, which indicate the structural variation due to the disease condition. Zernike moments are shape descriptors which can be used as prominent tools as they provide the rotation invariant features [8]. SVM classifier uses various types of kernels to create a decision boundary in the form of a hyperplane and is used to classify ASD and TD using the extracted features.

In this study, the DRLSE method has been used to segment brainstem region from sMRI. The best features from the feature space of segmented regions have been selected and a classification model is trained with optimizations, to aid in the diagnosis of ASD. The rest of the paper includes 3 sections- Section 2 discusses the method used in detail, section 3 describes the results with some discussion about all aspects of the methodology. Finally, section 4 outlines the results with some concluding remarks.

2. Method

2.1. Dataset

The public database Autism Brain Image Data Exchange (ABIDE-I and ABIDE-II) [9] was accessed to obtain sMRI data. The database is classified on the basis of Diagnostic and Statistical Manual of Mental Disorders–Fourth Edition (DSM IV) standards. TD and ASD subjects, 300 each, were carefully chosen to minimize the age difference. The demographics have been shown in Table 1.

Table 1. Participation information of sample set

	Mean ± SD (range)	
	ASD (N=300)	**TD (N=300)**
Males (Females)	260 (40)	223 (77)
Age in years (range)	11.87 ± 2.75 (6.41 - 18)	11.85 ± 2.74 (6.36 - 18.8)
PIQ/FIQ (range)	105.48 ± 17.1 (53 - 149)	111.15 ± 13.75 (62 - 147)

*PIQ/FIQ - Full-scale Intelligence quotient / Performance Intelligence quotient, *SD - Standard Deviation

The mid-sagittal view slices were considered for further processing. A few images with insufficient brainstem regions in the slices were discarded from our analysis.

2.2. Segmentation

The brain stem region is segmented from the sMRI using the DRLSE method [5]. By solving the gradient flow equation (equation (1)), the solution of the energy function is obtained.

$$\frac{\delta f}{\delta t} = \mu\left(d_p|\nabla f|\right) + \lambda\delta(f)\left(g\frac{\nabla f}{|\nabla f|}\right) + \alpha g\delta(f) \quad (1)$$

Here, g represents the gaussian gradient used for edge detection and to avoid the leakage of contours. The parameter values for the level set were set as α=1; μ=0.2; λ=0.1; number of iterations = 15. Trial and error were used to find these sets of parameters. Segmented images were validated against ground truth ones using five similarity measures - Simple Matching, Sokal and Sneath II, Hamann, Rogers and Tanimoto, and Pearson and Heron II, each based on varying criteria.

2.3. Feature Extraction and Classification

The segmented brainstem images were used to extract **Geometrical features** (18), like area, perimeter, eccentricity, orientation, bounding boxes, etc., reported in pixels, coordinates, as well as coefficients. Ratio-metric features (91) [10] were derived from the geometrical ones leading to a total of 109 geometry-based features. **Zernike moments** are mappings of an image onto a set of complex zernike polynomials [8]. Multiple combinations of the order of polynomial (n) and the degree of repetition (m) gave a total of 122 Zernike moments features: 61 Amplitude based (A_{OH}), and 61 recording the Phase angle (Pi_{OH}). The statistical significance of each feature was tested before feeding these into the classifier, by performing normality test to test the nature of distribution, and then t-test and Kruskal Wallis tests for normal and non-normal distribution respectively. SelectKBest method from the scikit-learn library helps choose the optimal feature subset, by ranking features based on F-test, which are then fed as input to the SVM classifier. Scikit-Learn's GridSearchCV returns the best combination of parameters from the input parameter grid, based on the described metric scores. A cross-validation set was used for testing the various parameter combinations.

3. Results

Figure 1(a) and 1(e) represent the mid-sagittal MR brain view of ASD and TD participants respectively. DRLSE methods helped in the evolution of the final contour to properly highlight the brainstem, as shown in figure 1(b) and 1(f). Generalized DRLSE methods detected brain stem boundaries with considerable efficiency. The masked copy of brainstem from the MR images can be observed in figure 1(c) and 1(g) for ASD and TD subjects respectively.

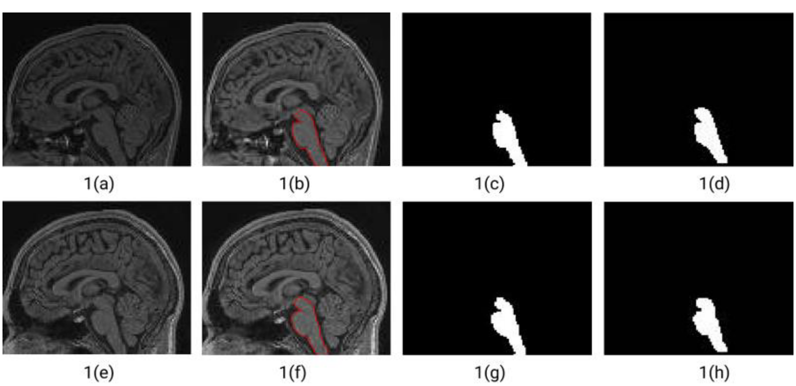

Figure 1. (a, e) Brain Image ASD, TD; corresponding (b, f) Final GDRLSE evolved contour; (c, g) Masked brainstem; (d, h) Ground truth binary image of brainstem

Medical Image Processing, Analysis, and Visualization software (MIPAV) was used to extract the brainstem region from the same dataset of sMRI. These ground truth images obtained can be visualized in figure 1(d) and 1(h) for ASD and TD subjects respectively. The ground truth images served as the validation set for brainstem extracted using the level set method. Validation of segmented brain stem image with the ground truth image using different similarity measures resulted in high correlation (Similarity Index nearer to 1).

The two measures, Pearson and Heron II (PH II), and Sokal and Sneath II (SS II) presented the highest correlation with a mean of 0.9740 and 0.9727 respectively. We calculated the geometrical and Zernike moments features from the DRLSE segmented brain stem images. 59 geometric and 32 Zernike moments features were found to be statistically significant, i.e. had a p-value < 0.05. The top 5 geometrical (including ratio-metric features) and Zernike moment features are presented in table 2.

Table 2.Top five significant geometrical and Zernike moments features

Geometric features	Zernike moments features
Eccentricity/Perimeter	n 7 m 3 A_{OH}
Area/Perimeter	n 12 m 8 A_{OH}
Minor Axis Length	n 17 m 17 A_{OH}
Centroid 2/Convex Area	n 8 m 2 A_{OH}
Convex Area	n 11 m 7 A_{OH}

The Ratio Eccentricity/Perimeter along with Zernike polynomial with the order of moments, n = 7 and the degree of repetition, m = 3 offered highest significance. The order is related to the number of concentric circular divisions, while the degree of repetition shows association with the number of circular sectors. SVM classifier was trained using different types of kernels – Linear, Polynomial, Sigmoidal and RBF. Out of these, the sigmoidal kernel performed best. With one of the five folds being used for testing and 4 being used for training, an accuracy of 70.53 % was reported. The Linear, Polynomial and RBF kernel elicited 58.92%, 57.39%, and 60% accuracy respectively.

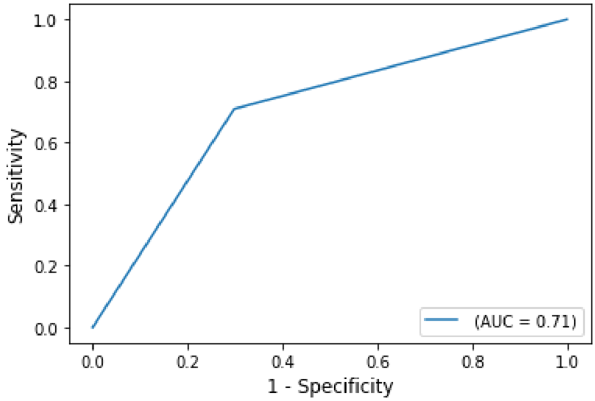

Figure 2. ROC-AUC Curve

The true positive rate (Sensitivity), is the ratio of true positives to the total positive ones, true negative rate (Specificity) is the ratio of true negatives to the total negatives and the F1 Score is the harmonic mean of precision (Positive predictive value) and sensitivity. The sensitivity, specificity and F1 score were reported as 0.6964, 0.7142 and 0.7027 respectively. The Receiver operator characteristics (ROC) curve demonstrating the Area under curve (AUC) can be visualized in figure 2.

4. Conclusions

This study describes the utility of geometrical and Zernike moments features extracted from the brainstem region for diagnosis of ASD. DRLSE based methods efficiently segmented the brainstem region, which was validated by the high similarity index obtained against the ground truth images. The features with the highest significance were obtained and used for classification of ASD from TD providing high accuracy, sensitivity and specificity. The study showed that shape-based features obtained with minimal manual intervention can be used to automate the diagnosis of ASD with relatively higher precision and much lower computational burden. Further work can be done by applying advanced deep learning methods for segmentation and classification of brainstem regions for ASD diagnosis.

5. Acknowledgement

This work was supported by the Science and Engineering Research Board through the Start-up Research Grant (SRG) scheme (SRG/2021/002289).

6. References

[1] Sinclair D, Oranje B, Razak K, Siegel S, Schmid S. Sensory processing in autism spectrum disorders and Fragile X syndrome—From the clinic to animal models. Neuroscience & Biobehavioral Reviews. 2017;76:235-253.
[2] Seif A, Shea C, Schmid S, Stevenson R. A Systematic Review of Brainstem Contributions to Autism Spectrum Disorder. Frontiers in Integrative Neuroscience. 2021;15.
[3] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 2013;
[4] Nguyen Duy T, Hino T. An improvement of interface computation of incompressible two-phase flows based on coupling volume of fluid with level-set methods. International Journal of Computational Fluid Dynamics. 2020;34(1):75-89.
[5] Li C, Xu C, Gui C, Fox M. Distance Regularized Level Set Evolution and Its Application to Image Segmentation. IEEE Transactions on Image Processing. 2010;19(12):3243-3254.
[6] Jac Fredo A, Kavitha G, Ramakrishnan S. Segmentation and analysis of brain subcortical regions using regularized multiphase level set in autistic MR images. International Journal of Imaging Systems and Technology. 2014;24(3):256-262.
[7] AR Jac Fredo, G Kavitha, & S Ramakrishnan, Analysis of corpus callosum and its sub- anatomical regions in autistic MR brain images using structure tensors,Second International Conference on Biomedical Systems, Signals and Images, IIT Madras, Chennai, India, 2016
[8] Hwang S, Kim W. A novel approach to the fast computation of Zernike moments. Pattern Recognition. 2006;39(11):2065-2076.
[9] Di Martino A, O'Connor D, Chen B, Alaerts K, Anderson J, Assaf M et al. Enhancing studies of the connectome in autism using the autism brain imaging data exchange II. Scientific Data. 2017;4.
[10] Suganthi M, Madheswaran M. An Improved Medical Decision Support System to Identify the Breast Cancer Using Mammogram. Journal of Medical Systems. 2010;36(1):79-91.