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Diagnosis of Autism Spectrum Disorder using Cortical Thickness Measures from Structural Magnetic Resonance Brain Images

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Abstract —*Early detection and diagnosis of autism would help in improved monitoring of therapy and life expectancy. This research work is concerned with developing a improved Computer Aided Diagnosis (CAD) system of autism spectrum disorders (ASDs). The proposed system utilizes the features, viz., cortical thickness measures for effectively classifying autistic and healthy brain images in an early stage. The preprocessing of sMRI is carried out using Statistical Parametric Mapping (SPM). The classification of autistic and normal brain images is performed using support vector machine. The experimental results prove that the proposed ASD system gives good performance in terms of sensitivity, specificity and classification accuracy.*

Keywords-*autism spectrum disorder; cortical thickness; computer aided diagnosis; brain images; classification*

I. INTRODUCTION

According to a survey, Autism spectrum disorders (ASDs) impact one out of every 100 children new born today. Diagnosis of Autism spectrum disorder is still challenging in India due to unsolved issues because of variety in severity and range of signs and symptoms. Autism is an extremely variable neuro developmental disorder that first develops during infancy or childhood, with strong genetic underpinnings and generally follows a constant course without exemption. The functional brain characteristics of autism during the time when symptoms first appear, namely during the 12-36 months, is almost fully unexplored. This is because MRI studies have been operated almost entirely with high functioning adolescents and adults with autism. With the relatively recent advent of modern brain imaging techniques, translational psychiatric research has embraced the systematic study of ASDs using these measurement tools to gain insight into the pathophysiology and possible etiology of ASDs. The ultimate promise of these approaches is to improve mechanistic accounts of ASDs as well as provide targets for novel intervention approaches.

The investigation and analysis of autism in neuro images of infants will aid in diagnosis, prognosis, and treatment decision-making. Imaging features may also aid to predict the common brain neuropathology that the autistic individual have or how the autistic individuals are responding to the treatment strategies [12]. Computer assisted intelligent medical image analysis methods can provide effective analysis tools to help the quantitative and qualitative clarification of medical images for differential diagnosis, intervention, monitoring and treatment of medical disorders. Quantitative feature extraction from the neuro images may also provide as a metric for biological efficacy of potential behavioral or pharmacologic interventions. This research work intends to use computational intelligence techniques to design and develop improved technique to effectively diagnose autism and help in the differentiation of autistic individuals from healthy individuals at an early age.

This research work would contribute in development of computational mathematical methods for solving problems applicable to medical images and their benefits for biomedical research and clinical care. The work will also be helpful in understanding physiological processes that correlates with the ASDs disease and its response to a treatment. The developed methodologies can be used to cure many medical problems associated with or aggravating autistic traits, that can be overcome to a variable extent, and to enhance quality of life of children with autism, though cure may not be available due to the inborn multi-genetic problem. The rest of this paper is organized as follows. Section II gives a brief description of related work carried out in the recent past. Section III describes the proposed methodology in detail. Section IV gives the obtained experimental results. Section V gives the concluding remarks.

II. FORMATTING YOUR PAPER

In recent years a lot of work has been carried out in diagnosis of autism spectrum disorder. These works clearly indicate that many advances have been made in various research aspects of ASD including classification, feature extraction and segmentation of the whole brain analysis. This section gives a review of most relevant contribution for diagnosis of autism spectrum disorder.

A novel approach to extract individual subject features from inter-regional thickness correlations based on structural magnetic resonance imaging (MRI) has been proposed in [10]. These features were used in a machine learning framework to obtain individual subject prediction of a severity scores based on neurobiological criteria rather than behavioral information. The structural covariances among several brain regions are associated with the presence of the autistic symptoms. Indices for inter-regional thickness correlation (IRTC) are estimated using Pearson correlation

between the cortical thicknesses of each region. In order to build a non-linear prediction model, support vector regression with radial basis function (SVR) is applied.

Cortical thickness analyses were performed using the Matlab based program SurfStat in [1]. The statistical analysis was performed at each vertex of the cortical surface using linear models to examine the differences in cortical thickness between groups controlling for both sex and age and interaction analyses to assess age-related changes between groups by regressing cortical thickness against age, controlling for sex. The differences in cortical thickness examined in relation to symptomatology and their association with age in the ASD group. Analyses were conducted using a general linear model, controlling for sex. The importance of including age interactions was underscored when analyzing structural properties of the autistic brain, as age effects may contribute to variance in structural indices.

In [4], a study was conducted in using cortical thickness measures for the first time to examine the relationship between ASD traits and cortical thickness in both ASD and TD (Typically Developing) adults. The continuous correlations was found between AQ scores and reduced cortical thickness across the ASD and TD groups in social brain regions and the default mode network including the medial orbitofrontal cortex, central sulcus postcentral gyrus and lingual gyrus. An inverse correlation was also found between cortical thickness in postcentral gyrus and AQ score.

III. PROPOSED METHODOLOGY

The Proposed System is designed to extract the cortical thickness of the sMRI image voxel by voxel to classify the autistic and healthy for the diagnosis of ASD. The preprocessing is done using SPM12 tool. From the preprocessed image cortical thickness measures are extracted as the features. The cortical thickness is fed into the SVM to classify the autistic and healthy brain. Figure 1 describes the proposed system for the Computer aided diagnosis of ASD. It consists of three stages viz., preprocessing using SPM, extraction of cortical thickness measures and classification of these features using SVM.

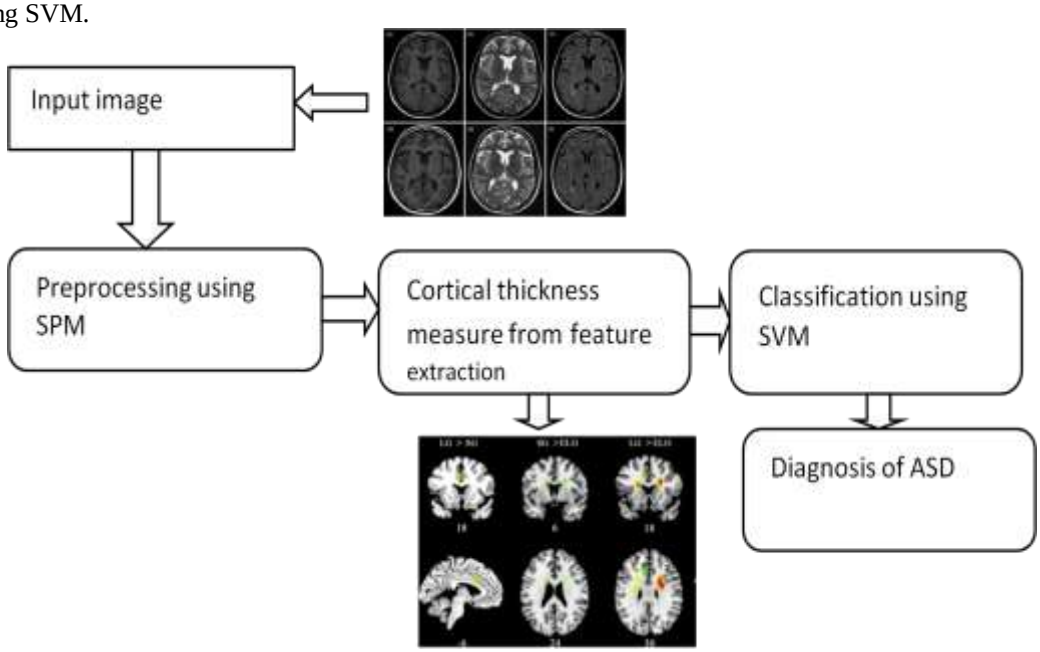

Figure 1 Proposed Methodology to diagnose ASD

3.1. Preprocessing using SPM

First, all T1-weighted images were manually realigned to the template. Then the realigned images were preprocessed using normalization. The realign option is used to give the source image in the normalization process. In the realign option, the source image has to be given in the data field, and then set the resliced images field as mean image only. This realigned image can be given as input to the source image in the normalize option. In the normalization option, the template field is set as 'EPI + nii' file. The resulting normalized images are 216 x 256 x 291 voxels representation for each subject.

3.2. Cerebral Cortical Thickness measures

The cortex has a surface area of on average 2.5 square feet, with a normal thickness of about 3mm. Measuring cortical thickness is an important task for both normal and abnormal neuro anatomy. The cortical mantle varies in thickness depending on the region of the cortex, with considerable variation between individual brains as well as between hemispheres of the same brain. In normal brains the cortex tends to be thinnest in the calcarine cortex at around 2mm and highest in the precentral gyrus at around 4mm [11]. Thickness information is thus both interesting in its own right as well as a useful aid in such tasks as sulcal labelling. In pathological cases cortical morphology has been known to vary in epilepsy, mental retardation, Schizophrenia, anorexia nervosa, autism and Alzheimer's disease. Moreover, it has been

shown that there is a general pattern of cortical evolution with age consisting of widening of the sulci along with a thinning of the cortical mantle [13]. This study clearly suggests that morphological changes in the thickness of the cortex are associated with meaningful functional differences across groups of normal and autistic person. The cerebral cortex should not be considered as a homogenous and indistinguishable mass of grey matter, but instead should be treated in terms of its laminar and columnar functional organisation.

Most of the brain data will come from Magnetic Resonance Imaging. The first and most obvious limitation is the inherent resolution of an MRI volume is that the best one can expect in a real dataset is one millimetre isomorphic sampling, though it might be possible to acquire 0.5 millimetre datasets for verification purposes. Even at 0.5 millimetres, however, individual neurons are clearly not visible and even the cortical layers are next to undifferentiable. The cortex in a structural MR image thus becomes a seemingly homogeneous grey mass; the finer points of anatomy that were delineated above disappear. The task of a thickness metric is thus to mathematically approximate those features in the absence of them actually being visible.

3.3. Classification using Support Vector Machine

Support Vector Machine (SVM) is one of the supervised learning methods for classification which defines the decision boundaries based on the concept of decision planes [2]. A set of objects having different class memberships are separated is decision plane. It is the effective supervised software tool widely used to obtain feasible solution with good generalization capability. Several studies [6, 7] have demonstrated the high performance accuracy of using SVM to detect autism. The distinct subject predictive information provided by the SVM classifiers allows the possibility to focus on the most discriminate areas of the brain in a case-control study which can be complemented with an anatomical description of the brain involvement in that particular pathology.

IV. EXPERIMENTAL RESULTS

The SMRI scans used in this study were from the ABIDE dataset provided by Di Martino et al [7]. ABIDE is an openly obtainable database that involved 16 international sites. ABIDE includes data from 532 individuals with ASD and from 573 individuals who were typical controls. All these 1112 datasets collected MRI (functional and structural) and phenotypic information for each subject. The ABIDE website is http://fcon_1000.projects.nitrc.org/indi/abide/ which describes the scan procedures and parameters [3][8]. The data available in the website is based on considerable variation SMRI acquisition protocols across sites and from the data of children and adolescents from three participating institutions. Totally 79 datasets are used in this study which are obtained from the sites Yale Child Study Center and University of Leuven, Belgium and Ludwig Maximilians University Munich, Germany. Out of 79 datasets, 40 were the individuals with ASD and the other 39 were of healthy individuals. The age group of the considered dataset for this study is below nine years. This age group was considered in this study, because early diagnosis would help in the treatment of the disease. The whole brain coverage of the MR acquisition, were the inclusion criteria for subjects within the chosen sites contain successful preprocessing with manual inspection of the MPRAGE images, and accurate realignment between the modalities. Each data sample contains, a high-resolution T1-weighted anatomical image (MPRAGE) of Structural MRI.

In the present work, classification of brain MRI images of autistic and healthy individuals is performed from the extracted cortical thickness measures. The proposed method involves three steps viz., 1) preprocessing through SPM 2) extraction of cortical thickness measures and 3) classification. In order to evaluate the performance of the proposed method, it is compared with an existing method which also involves three steps viz., 1) preprocessing through SPM 2) extraction of features through principal component analysis (PCA) and 3) classification.

Table 1: Sensitivity, Specificity And Classification Accuracy Values Using Hold Out Cross Validation Of The Proposed Method

Hold out Percentage	Sensitivity	Specificity	Classification accuracy
30	0.9091	1.0	0.9545
50	0.9474	1.0	0.9737
80	0.9677	1.0	0.9836

Table 1 illustrates the sensitivity, specificity and classification accuracy values obtained using 'Hold Out' cross validation of the proposed method. The Hold Out validation method divides the data into two subsets one for training and the other for testing. Three different grouping for training and test data viz., 1) 30% of training data and 70% of test data 2) 50% of training data and 50% of test data and 3) 80% of training data and 20% of test data are considered. It is appropriate to implement a cross validation scheme and to ensure an unbiased estimate of the classifier performance, both in the model selection phase and in the final evaluation of the classification accuracy using cortical thickness features.

In the table 1 the classification accuracy ranges from the 0.95 to 0.98 depending upon the Hold out percentage. The specificity range remains constant. The sensitivity of the cortical thickness in the performance measure ranges from 0.90 to 0.96.

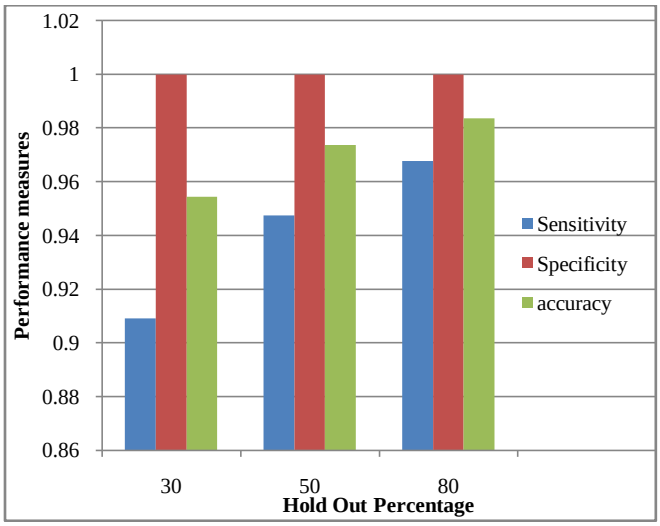

Fig. 7: Sensitivity, specificity and classification accuracy values related to the Hold out percentages

V. CONCLUSION

A computer aided diagnosis method using cortical thickness measures from the sMRI images is proposed in this paper to classify autistic and healthy brain images. In the first stage preprocessing of sMRI images is performed using SPM. In the second stage, the features viz., cortical thickness measures are extracted from the preprocessed sMRI images. These features are extracted from both healthy and autistic brain images obtained from the ABIDE database. SVM is used to classify the healthy and autistic individuals. The cortical thickness measure, which is obtained from feature extraction in this work, is well suitable in the diagnosis of ASD at the early stage. The classification accuracy of the proposed method for the autistic and control SMRI scans is 97.37%. The results are also promising in terms of sensitivity and specificity.

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