Radiomic analysis of brain MRI: A case study in Autism Spectrum Disorder

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Abstract

This work is intended to study the relationship between the morphology and texture of different brain structures and the presence of the disease called Autism. For that, it is proposed a radiomic analysis of the brain structures, amygdala and hippocampus, that will be performed by feature extraction and further analysis of the changes that occur in patients diagnosed with autism. Through the analysis of the textural features, it is expected the discovery of potential biomarkers that when combined with the morphological information, will possibly assist the diagnosis and a better understanding of Autism.

1 Introduction

Autism Spectrum Disorder (ASD) is a disease that develops in children, usually between 2/3 years old, being characterized by motor, cognitive and emotional difficulties. The causes of this disease are not yet fully understood, which has led to an increase in the study of this disorder. Recent studies indicated that the development of autism can cause structural and functional changes in the amygdala and the hippocampus, which are brain structures that are responsible for controlling some emotional and cognitive behaviours. For this reason, an effort has been made to understand the changes in those structures with the development of autism [1, 2]. One of the imaging approaches to visualize the changes that occur in brain structures is the Magnetic Resonance Imaging (MRI). Through this technique, 3D brain images can be acquired enabling subcortical quantitative analysis with focus on the amygdala and hippocampus. Once the images are obtained, features can be extracted from them, allowing a posterior analysis [1]. The extraction and mining of a high number of quantitative features in an automated and high-throughput way is called radiomics [1, 3]. Regional variations of texture in an image can be analysed in order to provide information about the brain structures in study. Its analysis is done through techniques dedicated to the quantification of the spatial variation of the gray tones of the image [4]. To the best of our knowledge, some of the existent studies in this field are contradictive, for example some conclude that in patients diagnosed with autism, there is an increase in the volume of the mentioned structures, while others indicate the opposite [5, 6].

The present work has the goal to find biomarkers capable of diagnose ASD. In order to achieve it, two approaches were followed: a first and general approach, by exploring the mean values of the features extracted from the MRI images, and a second approach done through a radiomics analysis of classification based on a similar study performed by Chaddad *et al* [1].

2 Methods

The data used was obtained from ABIDE I database, that provide MRI images gathered from several medical institutions around the world. A sample of 48 patients was used for this study, in which 24 were apparently healthy, being used as control and 24 were diagnosed with autism. In what concerns the age, only 10 had less than 15 years in which 5 had autism. Regarding the gender, 37 patients were male and 11 female. It is important to notice that the number of patients with different genders and ages was already determined in the samples taken from ABIDE I, not being determined within this project. The procedure was divided in three steps: (1) brain images segmentation, (2) feature extraction and (3) feature analysis.

2.1 Brain Images Segmentation

The MRI images obtained from the database were submitted to the VolBrain online segmentation workflow, capable of segmenting the brain into several structures (e.g. amygdala, hippocampus, cerebellum, cortex, etc) [7].

2.2 Feature extraction

The segmented images obtained from VolBrain were submitted to LifeX, a software capable of extracting morphologic (volume) and texture features taken from the gray-level co-occurrence matrix (GLCM) and histograms of each structure of the brain [8]. Six features obtained from the GLCM were extracted: energy, entropy, contrast, correlation, homogeneity and dissimilarity. The energy measures the homogeneity by the sum of squares of entries in the GLCM , the entropy represents de disorganization of the gray levels, the contrast symbolize local variations of the image intensity, the correlation represents the linear gray-level reliance between pixels and the homogeneity detects the similarity between the gray levels [9]. From the histograms, four features were extracted: skewness, kurtosis, entropy and energy. The skewness is a feature that gives information about the symmetry of the histogram and the kurtosis gives information about its flatness [9].

2.3 Feature analysis

Two types of feature analysis were performed. The first analysis carried out was a general exploratory approach, which may not be indicative of anything, since it was done through the observation of the mean values of the features. The main goal of this approach was to have a first look on the behaviour of the features, being analysed the quantitative difference between the average value of the same feature between cases and controls and also between age groups (<15 and > 15 years).

The second approach was done through case classification based on the feature space. The case classification using features both from the amygdala and hippocampus, were performed with three different models: support vector machine (SVM), neural networks (NN) and random forest (RF). In the non-linear SVM the radial basis function was used as kernel and in the linear SVM the linear function was used as kernel. Furthermore, in the SVM and NN models, the data had to be separated in training and testing and two different methods were used: the k-fold and the leave one out (LOO). Since that the RF classifier already does the separation of the data into training and testing, it was not necessary to apply the LOO or the k-fold methods, as in the other classifiers used. The k-fold method consists of dividing the total data set into $\boldsymbol{k}$ subsets of the same size and, from there, a subset is used for testing and the remaining $\boldsymbol{k}$-1 are used to estimate the parameters. This process is performed $\boldsymbol{k}$ times by alternating the test subset. The LOO method is similar to the previous one but instead of dividing the data into folds, it leaves only one example for test and the rest is for training. Thus, the process is carried out $\boldsymbol{N}$ times, equal to the number of sample sets [10]. The performance of the models was evaluated by their accuracy, obtained from the confusing matrix. The classification was performed in three different types of data: (a) features extracted only from the hippocampus, (b) features extracted only from the amygdala and (c) features extracted from both amygdala and hippocampus. Another relevant characteristic of the RF classifier is the possibility of measuring the importance of each feature on the classification process, allowing to rank them. This ranking was performed in 15 runs, allowing the obtaining of the TOP features in the classification of each data (a, b and c).

3 Results and discussion

Figure 1 presents the images obtained from the LifeX software, where it is possible to see the structures in study that resulted from the segmentation.

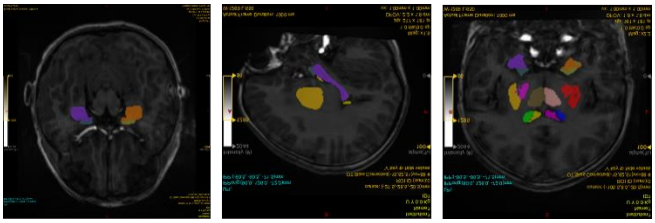

Figure 1: Frontal, sagittal and inferior images of the brain, highlighting the structures in study.

From the first exploratory analysis of the features, the average values of the volume of the two structures of the brain, separated by age and diagnostic were obtained and are represented in Table 1. It is possible to verify that in patients under the age of 15 years, both structures have a lower volume when compared to individuals of the same age range without autism. The same happens when comparing the volume of the hippocampus between individuals with autism and controls, over 15 years. However, in this age group it appears that the volume of the amygdala in individuals with autism is higher than that of controls.

Table 1: Volume (cm^3) of both studied structures of the patients (with and without autism) that participate in this study.

Age	Patients with autism		Controls	
	Amygdala	**Hippocampus**	**Amygdala**	**Hippocampus**
<15	2.09	9.94	2.47	10.21
>15	1.56	9.50	1.02	9.72

The same exploratory analysis was carried out with the textural features. Regarding the textural characteristics obtained from the histograms, it was possible to verify that the hippocampus in patients with autism presented higher values of skewness, kurtosis and entropy and lower energy than in patients without this disorder. The same features taken from the amygdala of patients with autism presented lower values of skewness and kurtosis and higher values of entropy and energy. The same analysis made of the textural features taken from the GLCM in the hippocampus showed, in patients with autism, lower values of homogeneity, energy, contrast, correlation and dissimilarity and higher values of entropy. In the amygdala, the same analysis showed higher values of homogeneity, correlation, entropy and dissimilarity and lower energy and contrast in patients with autism. The same analysis was done separating the sample in age groups (<15 and > 15 years) however, it was not found a general rule to the behaviour of the features. It should be noticed that this analysis is only exploratory, and the quantity of patients used should be larger in order to obtain more conclusive results. Also, the number of patients under 15 years used for this study was significantly less than the patients above 15 years, giving only a general idea of the differences in the age groups.

Through the second approach of the analysis of the features, the accuracy of each classifier used were obtained, being possible to evaluate each one of them. The results obtained are shown in Table 2.

Table 2: Accuracy values of each model used to classify the data used, for both LOO and k-fold split methods.

	Hippocampus		**Amygdala**		**Hippocampus + amygdala**	
	LOO	**kf**	**LOO**	**kf**	**LOO**	**kf**
SVM linear	0.500	0.575	0.625	0.575	0.625	0.642
SVM non linear	0.500	0.592	0.563	0.625	0.500	0.500
NN	0.604	0.592	0.500	0.567	0.688	0.633
RF	0.958		0.958		0.980	

It should be noted that a greater accuracy was obtained with the RF model in all the data used, both with the LOO method and with the k-fold to separate the data in training and test datasets. The LOO method is computationally expensive, which in this case does not represent a problem because of the small size of the sample [10]. However, if the study was projected in a bigger sample, preference would be given to the k-fold method. The dataset containing characteristics of the amygdala and hippocampus had better results compared to the data containing only characteristics of the amygdala or the hippocampus. This may indicate that by analysing the structures together, it is possible to obtain better results in classifying patients with autism using this models.

For each set of classified data, the TOP features were obtained after 15 runs, as mentioned before, and are represented in Table 3. Firstly, it should be noted that the features extracted from the GLCM are those that allow a better classification of the structures, since they appear with more frequency compared to the ones extracted from the histograms. It is possible to verify that the volume of the amygdala, entropy, homogeneity and dissimilarity are the most common characteristics of the 3 data sets. This way, it is possible to conclude that these features can be used as biomarkers to identify autism.

Table 3: TOP features obtained through the RF classification model for each data set used.

Amygdala	**Hippocampus**	**Hippocampus + amygdala**
Age	Homogeneity (GLCM)	Amygdala volume
Volume	Energy (GLCM)	Amygdala entropy (GLCM)
Contrast (GLCM)	Entropy (GLCM)	Hippocampus homogeneity (GLCM)
Correlation (GLCM)	Dissimilarity (GLCM)	Hippocampus entropy (GLCM)
Entropy (GLCM)		
Dissimilarity (GLCM)		

4 Conclusion

This work intended to analyse MRI brain images, in particular the hippocampus and amygdala structures, in order to contribute to the diagnose and understanding of the ASD. This was possible through a radiomic analysis of the MRI images, extracting texture and morphologic features and analysing them by two different approaches. This way, it was possible to compare those feature between patients with and without autism. The first approach allowed the general understanding of the behaviour of the features and the second approach allowed us to achieve the features that presented more potential to become biomarkers in the diagnosis of ASD. In order to achieve this in the second approach, several feature classification models were used and evaluated through their accuracy, allowing to achieve the conclusion that the RF model presented better results in classifying the patients in cases or controls. It was also with this model, that was possible to obtain the features with more potential to be used as biomarkers in the diagnosis of autism.

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