

Brain Volume Analysis with T1-MRI Data in Autism Spectrum Disorder

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Abstract

Purpose: Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that is characterized by impaired social interactions. Early detection can prevent the progression of the disease. So far, much research has been done to better diagnose autism. Investigation of brain structure using Magnetic Resonance Imaging (MRI) provides valuable information on the evolution of the brain of patients with autism.

Materials and Methods: In this study, we equally selected T1-MRI data from 20 control subjects and 20 patients, aged under 13 years (male and female, right hand and left hand). MRI research has shown that the brain of autistic children has grown locally and globally. In this paper, for the brain volumetric evaluation of autistic patients, the MRI data was segmented and then analyzed with a statistical method, which has been investigated more generally, in both the cortical and subcortical areas.

Results: We extracted 110 cortical and subcortical brain areas. The statistical analysis show which areas are important in discriminant between ASD and healthy control groups. According to the results of MRI, an increase in overall growth is seen in the subcortical areas of the brain (amygdala and hippocampus) as well as the cerebellum, but in adults with autism, a decrease in brain volume is seen.

Conclusion: In this study, we analyze the T1-MRI data of ASD subjects for early detection of Autism disorder. Our results were shown in the 6 brain areas that have P-values under 0.005. These areas are important in the early detestation and treatment of ASD.

Keywords: Autism Spectrum Disorder; Magnetic Resonance Imaging; Autism; Statistical Analysis.

1. Introduction

Autism Spectrum Disorder (ASD) is a mental and neurodevelopmental disorder that is characterized by impaired social interactions, communication, repetitive behaviors, limited interests, and delayed movements such as sitting, walking, and so on [1]. The most significant social deficits in autism include the inability to communicate with the eye, lack of emotion, social interactions, disability in nonverbal behavior, and age-related communication and verbal communication behaviors in these patients are abnormal [2, 3]. It is considered a spectrum because of the variety and heterogeneity of autism manifestations [4]. For example, the collection of autistic children with an IQ below 40 and another group with impaired communication and social interactions are individuals with very high IQ and are considered geniuses [5]. Studies have shown that social brain activity causes social interactions. The social brain includes parts of the brain, including the amygdala, hippocampus, anterior temporal lobe, and so on [6, 7]. Since the amygdala has a fundamental role in socio-emotional behaviors, it is a major neuronal region in pathophysiological autism [8]. Anatomical abnormalities can also be referred to as pathophysiological autism in that brain growth is excessive and abnormal at birth but decreases sharply in adolescence and adulthood [2]. The disease is more common in boys than in girls, such that one in every 42 boys and one in 189 girls having autism [9]. There has been a lot of controversy in the field of autism, the results obtained are that genetic and environmental factors or a combination of both are effective in this disease [10]. Cognitive, behavioral, and verbal states of autism usually appear in the first three years of a child's life and are not detectable before, and in fact, the opportunity to prevent the progression and treatment of the disease is lost during this period [11, 5]. Therefore, early detection can prevent the progression of the disease. So far, much research has been done to better diagnose autism [12]. Investigation of brain structure using MRI (magnetic resonance imaging), which is a non-invasive procedure, and since there have been advances in structural and functional MRI techniques, thus provides valuable information on the evolution of the brain of patients with autism [13, 14]. Functional MRI-based research describes functional changes in the brain and the relationships between different areas of the brain in autistic patients. It found that the

relationship between posterior frontal areas decreased and there was a direct relationship between decreased cerebellar gray matter activity and decreased communication and interactions of children with autism [14, 15]. On the other hand, results from Structure MRI research have shown that the brain of autistic children has grown locally and globally [14], and this increase in brain volume is due to an increase in the gray matter [16, 17]. Volume is an important feature of the brain, and volumetric MRI imaging is one of the methods used to analyze the volume and structure of the human brain [18]. Therefore, in this paper, for the brain volumetric evaluation of autistic patients, the method of processing MRI of the brain has been investigated more generally in both the cortical and subcortical areas.

2. Materials and Methods

2.1. Data Acquisition

The renewed repetition of the Autism Brain Imaging Data Exchange (ABIDE II) was performed to enhance the extent of brain communication research in Autism Spectrum Disorder (ASD) [19]. According to the initial ABIDE effort (ABIDE I), which released 1112 datasets in 2012, the new data source is a collection of resting functional Magnetic Resonance Imaging (MRI) and structural MRI data and phenotypic data [19]. ABIDE II consists of 17 independent data sets with 487 data sets as ASD and 557 as control. These represent collected from 7 international institutions. Also, ABIDE II includes a wide range of psychiatric variables for our understanding of neural psychiatric communication and 284 diffusion imaging data sets. All collections include data from both sexes and the average age is 11.7 years [19]. 15% of whom were autistic women and 31% of the control group, and the rest was autistic men. For both groups, the mean Full-scale Intelligence Quotient (FIQ) is above average so that 97% of the datasets FIQ are above 80. In this paper, we equally selected data from 20 control subjects and 20 patients, aged under 13 years (male and female, right hand and left hand). For each of the collections minimum of one MRI and the resting-state functional Magnetic Resonance Imaging (fMRI), datasets are existent. The Neuroimaging Informatics Technology Initiative (NIFTI) template was selected to store data from the MRI ABIDE II data set. All MRI data were obtained using 3 Tesla scanners. To achieve all the data, a 3D MPRAGE sequence

(three-dimensional magnetization prepared rapid acquisition gradient echo) or a special type of vendor has been used. The sequence of MRI parameters includes the following:

BW, bandwidth per pixel; Dims, dimensions; ES, echo spacing; FA, flip angle (indexed in degrees); PA, parallel acquisition; PE, phase encoding; PF, partial Fourier (half scan); SO, Slice orientation; TA, Acquisition Time; TE, Echo Time; TI, Inversion Time; TR, Repetition Time; For parallel acquisitions; SS, SENSE acceleration in the slice direction; SP, SENSE acceleration in the phase encoding direction; GP, Gene Ralized Autocalibrating Partial Parallel Acquisition (GRAPPA) acceleration in the phase encoding direction; AP, ASSET acceleration in the phase encoding direction. For partial Fourier, the under-sampled dimension is listed with the under-sampling factor; P, phase encoding. For slice orientation; S, sagittal; T, transverse (axial); C, coronal. For phase encoding direction; RL, right-to-left; AP, anterior to posterior [19].

2.2. The Processing

In the first stage, all T1-MRI data were pre-processed with Statistical Parametric Mapping (SPM) version 12, which runs on MATLAB to eliminate noise and artifacts such as Anatomical MRI Segmentation, and spatial smoothing. In the next step, the data transformed into the Montreal Neurological Institute (MNI) space and defined the brain areas. The data was segmented to cortical and subcortical areas for extracted cortical and subcortical thickness. Finally, for selection, the best features for the volumes of brain area group analysis of the data was done. The best features were selected using filter methods by calculating a score for each feature with statistical methods.

3. Results

The proposed methods were implemented in MATLAB 2019b. We extracted 110 cortical and subcortical brain areas. The statistical analysis show which areas are important in discriminant between ASD and healthy control groups. Figure 1 shows the univariate statistical test filter method for the decimation of the groups. The feature selection method calculates a score for all features and then select the

features with the lowest P-values scores. Our results were shown in several areas of the brain (Tissue grey matter; Cerebelume right, left and total; amygdala left and total) that have P-values under 0.005. These areas are important in the early detestation and treatment of ASD. Figure 2 shows the tissue classification in used T1-MRI data.

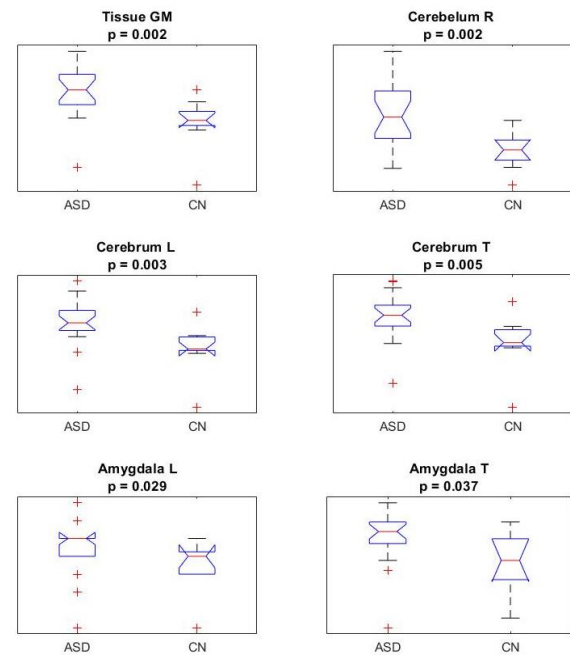


Figure 1. Results of statistical analysis for discrimination between ASD and healthy control groups using t-test. Declaring a test to be significant when P-value <0.05

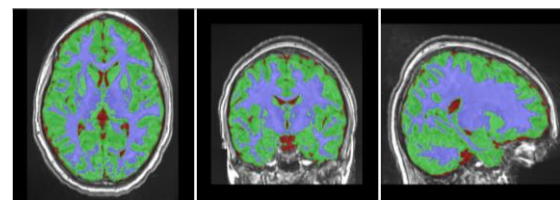


Figure 2. The tissue classification used T1-MRI data in three slice viewer, from left to right (Transverse, Coronal, and Sagittal view, respectively)

4. Discussion

In this study, we analyze the T1-MRI data of ASD subjects under 13 years of age for early detection and treatment of Autism disorder. The results showed that six areas of the brain, including Tissue grey matter; Cerebelume right, left, and the total; amygdala left, and the total; have the lowest P-values score. These areas are important in diagnosing autism.

In a review of recent studies on the association of structural MRI with autism, we found consistent patterns.

The amygdala has invariably been a favorite structure in the search for a neuropathological grading of autism, due to its important role in shaping the emotional and social behavior that is impaired in people with ASD [20]. In one study, an increase in gray matter volume in the amygdala and hippocampus was reported in people with autism under 18, as well as a decrease in gray matter in adult patients in these areas [1]. According to the results of MRI, an increase in overall growth is seen in the subcortical areas of the brain (amygdala and hippocampus) as well as the cerebellum, but in adults with autism, a decrease in brain volume is seen [21]. The left hippocampus and right amygdala are significantly larger than the control group in autism, which may be due to increased activity and thus perception and regulation of emotions [22]. Basal ganglia structures, including the putamen, are involved in many cognitive-motor functions as well as memory and learning. Putamen dysfunction is thought to lead to repetitive behaviors in people with ASD [23, 24]. On the other hand, the magnitude of striated structures such as left and right putamen and left caudate nucleus was found in the autism group [25]. The volume of the caudate nucleus is maximized in ASD, which results in Restricted and Repetitive Behaviors (RRBS) [26]. High-resolution structural brain scans were performed in autistic and healthy individuals, resulting in a significant increase in pallidum volume and lateral volume in autistic individuals compared to healthy individuals [27]. Neurons in the thalamus may control social behaviors and therefore be involved in autism. The circuit connecting the thalamus to the prefrontal cortex is important for social behavior [28].

Finally, we conclude that there are many conflicting findings in the study of autism with structural MRI. On the other hand, the performance of different diagnostic models is influenced by a variety of characteristics selected by researchers. However, many factors such as age, diagnostic criteria, analytical methods, and feature extraction methods may play a role in this difference.

References

- 1- Liu, J., *et al.*, “Gray matter abnormalities in pediatric autism spectrum disorder: a meta-analysis with signed differential mapping”. *European child & adolescent psychiatry*, 26(8): pp. 933-945, 2017.
- 2- Koshino, H., *et al.*, “fMRI investigation of working memory for faces in autism: visual coding and underconnectivity with frontal areas”. *Cerebral cortex*, 18(2): pp. 289-300, 2008.
- 3- Dickstein, D.P., *et al.*, “Developmental meta-analysis of the functional neural correlates of autism spectrum disorders”. *Journal of the American Academy of Child & Adolescent Psychiatry*, 52(3): pp. 279-289. e16, 2013.
- 4- Guo, X., *et al.*, “Decreased amygdala functional connectivity in adolescents with autism: a resting-state fMRI study”. *Psychiatry Research: Neuroimaging*, 257: pp. 47-56, 2016.
- 5- Jiujiyas, M., E. Kelley, and L. Hall, “Restricted, repetitive behaviors in autism spectrum disorder and obsessive-compulsive disorder: a comparative review”. *Child Psychiatry & Human Development*, 48(6): pp. 944-959, 2017.
- 6- Gross, C., “Defective phosphoinositide metabolism in autism”. *Journal of neuroscience research*, 95(5): pp. 1161-1173, 2017
- 7- Gotts, S.J., *et al.*, “Fractionation of social brain circuits in autism spectrum disorders”. *Brain*, 135(9): pp. 2711-2725, 2012.
- 8- Patriquin, M.A., *et al.*, “Neuroanatomical and neurofunctional markers of social cognition in autism spectrum disorder”. *Human brain mapping*, 37(11): pp. 3957-3978, 2016.
- 9- Baron-Cohen, S., “The cognitive neuroscience of autism”. *BMJ Publishing Group Ltd*, 2004.
- 10- Christensen, D.L., *et al.*, “Prevalence and characteristics of autism spectrum disorder among children aged 8 years—autism and developmental disabilities monitoring network, 11 sites, United States, 2012”. *MMWR Surveillance Summaries*, 65(13): pp. 1, 2018.
- 11- MacDonald, M., B. Hatfield, and E. Twardzik, “Child behaviors of young children with autism spectrum disorder across play settings”. *Adapted Physical Activity Quarterly*, 34(1): pp. 19-32, 2017.
- 12- Mohammadi, M.-R. and S. Akhondzadeh, “Autism spectrum disorders: etiology and pharmacotherapy”. *Current Drug Therapy*, 2(2): pp. 97-103, 2007.
- 13- Mahajan, R. and S.H. Mostofsky, “Neuroimaging endophenotypes in autism spectrum disorder”. *CNS spectrums*, 20(4): p. 412, 2015.
- 14- Hernandez, L.M., *et al.*, “Neural signatures of autism spectrum disorders: insights into brain network

- dynamics". *Neuropsychopharmacology*, 40(1): pp. 171-189, 2015
- 15- Ruggeri, B., et al., "Biomarkers in autism spectrum disorder: the old and the new". *Psychopharmacology*, 231(6): pp. 1201-1216, 2014.
- 16- Campbell, M., et al., "Computerized axial tomography in young autistic children". *The American Journal of Psychiatry*, 1982.
- 17- Hazlett, H.C., et al., "Magnetic resonance imaging and head circumference study of brain size in autism: birth through age 2 years". *Archives of general psychiatry*, 62(12): pp. 1366-1376, 2005.
- 18- Riva, D., et al., "Gray matter reduction in the vermis and CRUS-II is associated with social and interaction deficits in low-functioning children with autistic spectrum disorders: a VBM-DARTEL Study". *The Cerebellum*, 12(5): pp. 676-685, 2013.
- 19- Di Martino, A., et al., "Enhancing studies of the connectome in autism using the autism brain imaging data exchange II". *Scientific data*, 4(1): pp. 1-15, 2017.
- 20- Howard, M.A., et al., "Convergent neuroanatomical and behavioural evidence of an amygdala hypothesis of autism". *Neuroreport*, 11(13): pp. 2931-2935, 2000.
- 21- Li, D., H.-O. Karnath, and X. Xu, "Candidate biomarkers in children with autism spectrum disorder: a review of MRI studies". *Neuroscience bulletin*, 33(2): pp. 219-237, 2017.
- 22- Groen, W., et al., "Amygdala and hippocampus enlargement during adolescence in autism". *Journal of the American Academy of Child & Adolescent Psychiatry*, 49(6): pp. 552-560, 2010.
- 23- Hollander, E., et al., "Striatal volume on magnetic resonance imaging and repetitive behaviors in autism". *Biological psychiatry*, 58(3): pp. 226-232, 2005.
- 24- Estes, A., et al., "Basal ganglia morphometry and repetitive behavior in young children with autism spectrum disorder". *Autism Research*, 4(3): pp. 212-220, 2011.
- 25- Auerbach, B.D., E.K. Osterweil, and M.F. Bear, "Mutations causing syndromic autism define an axis of synaptic pathophysiology". *Nature*, 480(7375): pp. 63-68, 2011.
- 26- Qiu, T., et al., "Two years changes in the development of caudate nucleus are involved in restricted repetitive behaviors in 2-5-year-old children with autism spectrum disorder". *Developmental Cognitive Neuroscience*, 19: pp. 137-143, 2016.
- 27- Turner, A.H., K.S. Greenspan, and T.G. van Erp, "Pallidum and lateral ventricle volume enlargement in autism spectrum disorder". *Psychiatry Research: Neuroimaging*, 252: pp. 40-45, 2016.
- 28- Rikhye, R.V., R.D. Wimmer, and M.M. Halassa, "Toward an integrative theory of thalamic function". *Annual review of neuroscience*, 41: pp. 163-183, 2018.