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Source Localization based Healthcare Diagnostic System using ERP signals: An application to ASD

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Abstract—**Aim: Autism spectrum disorder is a complex disorder in which persistent challenges are introduced in communication, social interaction and repetitive patterns are introduced that affects 1% individuals in United Kingdom and 1.5% individual in united states. The number of individuals affected by autism is 1 in 110 in india and 1 in 68 worldwide. It has been estimated that 2 million people in India are affected by autism spectrum disorder.In this study we used Evented Related potentials(ERP) to investigate the brain area in order to diagnose ASD.**
Methods: This study enrolled 20 individuals with Autism and 20 typically developing individuals. Low-resolution electromagnetic tomography (LORETA) was used to analyze ERP data to reveal the mechanisms underlying Autism in individuals.
Results: There were significant difference in current density between Autistic and typically developing individuals. In the entire brain area, the occipital lobe concerned with visual perception exhibited the most significant difference between the individuals with autism and typically developing individuals groups. Differences were also observed in parietal and frontal lobes.
Conclusions: LORETA can prove to be a revolutionary tool for investigation of autism spectrum disorder.In comparison to other techniques ERP is a promising biomarker for autism . By comparing activation maps at different time instants one can diagnose Autism at a early stage Our study aims to address diagnostic approach for autism in individuals.

I. INTRODUCTION

Neuro-developmental disorders refer to the class of the disorders in which the brain dysfunctionalities occur with the growth of the individuals. The disorder manifest in early developmental age, even before the second birthday of child and are characterized by different deficits. The deficits are not limited to this but lead to motor skill impairment, verbal and non-verbal communication deficit, learning deficit and lack of interaction, memory and emotions. The list of the developmental disorder involves huge variations of symptoms and heterogeneity. The widely occuring neuro-developmental disorders are epilepsy (Bozzi et. al., 2012), Autism Spectrum Disorder (ASD), Attention Deficit Hyper Disorder (ADHD), cerebral palsy, intellectual disability, language disorders, communication disorder and dyslexia. These disorders can co-occur in themselves such as ASD with epilpesy, ASD with intellectual disability. These disorders are called developmental since some deficits keep on changing or developing with the age while some of them remain permanently in the individual. The subset of deficit is

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different for each and every individual making the individual unique in himself. This diversity in the nature of the disorder is the reason that the diagnosis as well as intervention is a very complex process [https://www.epilepsy.com/learn/about-epilepsy-basics/epilepsy-statistics]. The cause of the disorder has not been particularly defined but it is related with the neuro-developmental manifestations. These disorders are included in the Diagnostic and Statistical Manual of Mental Disorders (DSM) manuals and the DSM-5 [American Psychatric Association] is the latest one. The new edition of DSM-5 has combined these three diagnoses under the single diagnosis of ASD (American Psychiatric Association, 2013). The modification in the diagnostic manuals and techniques highlight the fact that neurodevelopmental disorders are complex disorders and for better diagnosis the approach needs to be based on multi-modal ways of detecting behavioral traits.

According to a report, in United States 15% of the individuals of age-group are suffering from neuro-developmental disorders. The number of individuals affected with autism are 1 in every 68 and in india it is 1 in every 110 [http://unstats.un.org/unsd/demographic-social/meetings/2016/bangkok- -disability-measurement-and-statistics/Session- 6/India.pdf].The number is very high and this is the reason of including autism disorder in to this thesis work. The range of epilepsy in United States is 5-8.4 in every 1000 or in lifetime it is 1 in 26 have suffered from epilepsy in their entire lifetime. The cases of disorders are getting more diagnosed day by day with the prevalence of much more techniques and ushering technology. There is no report of predicting that these disorders have only one symptom which can be the marker of the disorder. There is no cure of the disorder but definitely the disorder can be controlled and can be retraced to some extent with the help of medication and some therapies. These therapies and medication will be more effective only when the disorder is diagnosed at early period of its manifestation. The diagnosis and intervention technologies are on their way of better detection and treatment but till now there is no robust technique or marker which can diagnose these disorders at very early stages of life.

ASD is a disorder in the children present at birth time not any disease described by the triad of disorders: autism, Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS) and Asperger Syndrome (AS; Muñoz et al., 2012; Bouras, 1999; American Psychiatric Association, 2000). Rett syndrome and childhood degenerative disorder are also found in children but less frequently as compared to the triad of disorders (Matson et al., 2007). Autism is a persistent developmental embarked by spectrum of symptoms broadly classified in to three domains: (i) sparsity of social interaction, relations and enormous aloofness (ii) unable to communicate and share emotions, motor impairments and qualitative and quantitative language disability, (iii) repetitive activities, distressed behavior and constrained interests (Brandwein et al., 2015; Kanner, 1943; Tas et al., 2007). The uncertainty of symptoms can vary from individual to individual more or less and cannot be limited to any particular extent.

ERP(Event related potentials)have been used to detect various neurodevelopmental disorders in individuals.ERPs have high temporal resolution and can detect changes in a matter of milliseconds.ERPs are inexpensive and noninvasive tools which can help to clinically access changes in functional connectivity related to autism. In this paper ERP data of autistic and TD individuals was taken in the presence of visual stimuli.

Electromagnetic signals are generated during activation inside the brain.The localization of active sources inside the brain is termed as brain source localization.The process of estimation of active sources in the brain is termed as EEG based brain source localization.The process of EEG based source localization is helpful in understanding the functional,pathological,physiological abnormalities related to the brain.The brain source localization approaches are helpful in diagnosis of various neurodevelopmental disorders such as autism and epilepsy. There are different approaches available that are used to localize the active sources including LORETA, standardized LORETA,exact LORETA, minimum norm etc. In this paper brain source localization techniques such as Sloreta has been discussed.ERP dataset of subjects with visual stimuli at four different time instants in terms of activation maps, scalp map has been discussed in this paper.

A. Brain source localization techniques

S.No.	Method or Technique	Reference/Author	Advantages	Limitations
1.	Minimum norm solution[1]	Matti.S.Hamalainen(1984)	Current estimation and resolution are provided with good results	Localization error is introduced and deep source localization is not addressed
2.	LORETA[2]	RD PASCAL(1994)	Provides better capabilities for localizing deep sources	It provides low resolution with blurred images,which is highly undesirable for feature selection.
3	FOCUSS[3]	F.Irina.et.al(1995)	Non uniquely defined	It involves large

			sources are properly localized and provides stable outputs	mathematical calculations and involves large computational time
4	Recursive MUSIC[4]	J.C.Mosher(1998)	Recursive MUSIC provides low localization error with better estimation	Errors and noise increase the complexity of the algorithm
5	sLORETA[5]	R.D Pascual(2002)	Zero Localization Error	Low resolution imaging method.
6	Shrinking LORETA-FOCUSS[6]	He Sheng(2003)	Provides better localization as compared to sLORETA	It has limitation while using real time data
7	Hybrid weighted minimum norm[7]	C.Y Song.et.el(2005)	Provides in depth localization with less errors	Large computations which increase computational time
8	eLORETA[8]	R.D Pascual(2007)	Authentic localization technique with zero localization error	Low resolution feature causes blurring of images
9	WMN-LORETA[9]	R.Khemkhan(2008)	Hybrid technique which provides better localization than LORETA WMN alone	System is complex and requires high computational time
10	Recursive Sloreta and FOCUSS[10]	R.Khemkhan(2008)	More efficient in terms of localization and computational time	No validation provided.Results were produced on simulated data.

II. MATERIAL AND METHODOLOGY

A. Subjects

Two groups of participants were included in the study.17 TD individuals[1.5-25years] and 17 ASD patients[**2-20 years**] were a part of this experiments.ERP data was taken for comparison which was provided by Dr. Michaela Esslen, Institute of Neuropsychology, university of Zurich. Visual Stimulus in the form of pictures of flowers was provided to the participants.Electrodes taken were 25 with sampling rate of 256 Hz. For this study, different time instants were considered 253.906, 480.469, 42.968 ms.The results For recruitment of ASD individuals special schools of jalandhar were consulted.Parents and caretakers of autistic individuals were also consulted.

TABLE I. PARAMETERS USED FOR ANALYSIS

Features	**ASD**	**TD**
Number of individuals	20	20
Age	8-20	4-25
No of electrodes	25	25
Sampling frequency	256Hz	256Hz
Visual Stimuli	Pictures of flowers	Pictures of flowers

B. Data acquisition and processing

A Generation of activation maps

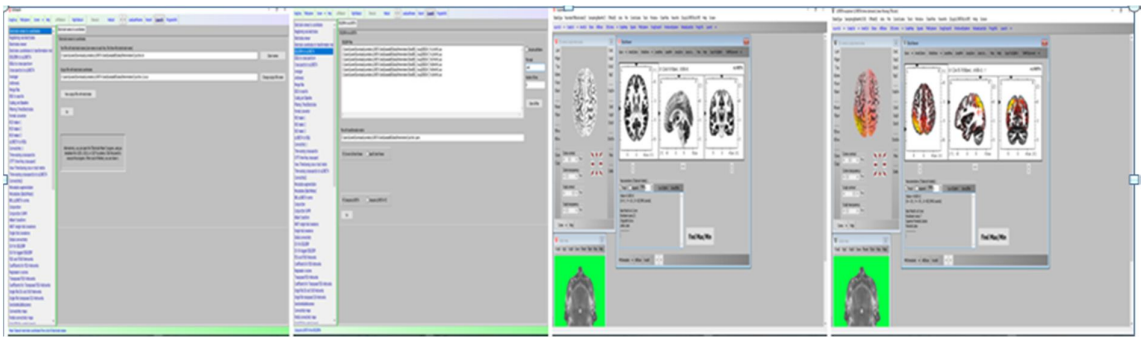
The methodology of source localization is carried out using sLORETA software. KEY Institute of Brain-Mind Research, Zurich Switzerland developed this software package. Data of young normal individuals was provided by Peter anderer, Professor of biomedical engineering.10-20 international system electrode international system is used for placing the electrodes. The data have following specifications: a ERP file was used with 5s worth of data, 25 electrodes were used in the dataset. The data set is of 20 young patients and 20 ASD patients in resting state.

Step1: The first step involves the conversion of .txt file to. sxyz file format.The sampling rate is 102.4Hz

Step 2:ERP data files(.asc) are entered along with the transformation matrix in the software utility.sLORETA file is selected from the utility window.

Step 3: After applying all the necessary transformations, sLORETA explorer utility is selected from the software.

Step 4: For visualization of activation,the selected data is examined at three different time instants.Slice viewer,3D cortex map and scalp map are examined and different activated regions are shown.



STEP 1 STEP 2 STEP 3 STEP 4

Fig 1 Steps for data acquisition and processing

III. RESULTS AND DISCUSSION

The results were taken using Sloreta utility and activation was observed at different regions of the brain according to the stimulus given at three different time instants.The activation maps generated are dependent upon the stimulus given and attention of the concerned subject. It was observed that maximum activation was observed in the occipital region in case of TD individuals while maximum activation was observed in parietal regions in case of ASD individuals. Occipital lobe is responsible for vision and visual tasks[2].Decrease in functional connectivity in task related regions is one of the promising biomarkers for detection of autism at a early stage.

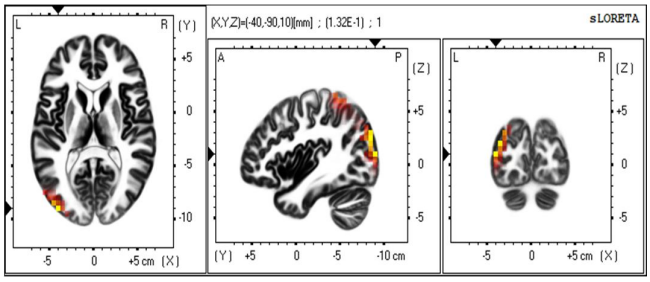


Fig 2.Activation map for TD individuals at 253.906 ms

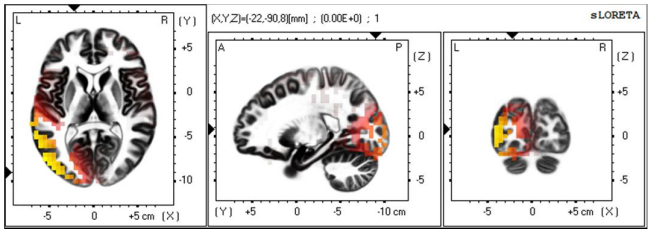


Fig 3.Activation map for TD individuals at 480.906 ms

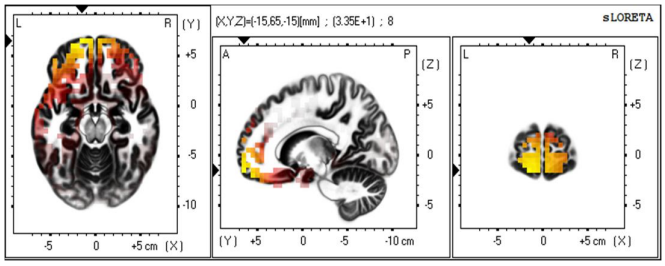


Fig 4.Activation map for TD individuals at 42.96 ms

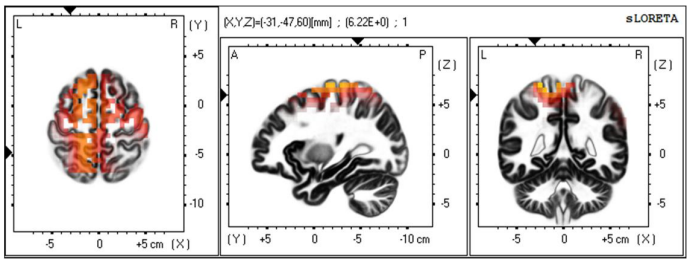


Fig 5.Activation map for ASD individuals at 253.906 ms.

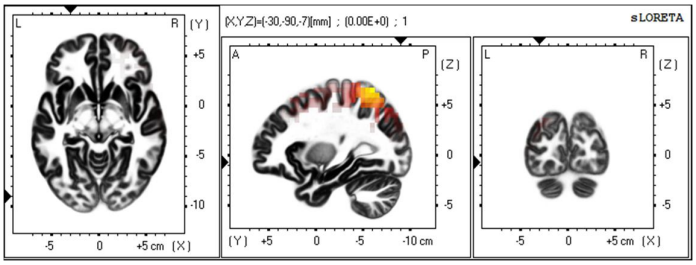


Fig 6.Activation map for ASD individuals at 480.906 ms

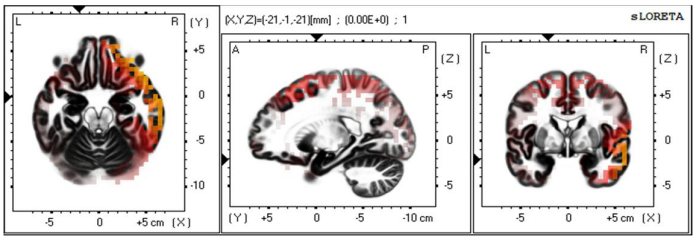


Fig 7.Activation map for ASD individuals at 42.96 ms.

TABLE II. COMPARATIVE ANALYSIS OF REGIONS AFFECTED

Type of individual	Time instant	Region with maximum connectivity
ASD	253.96 ms	Parietal Lobe
ASD	480.906 ms	Parietal lobe
ASD	42.96 ms	Frontal,Parietal
TD	253.96 ms	Occipital
TD	480.906 ms	Occipital
TD	42.96 ms	Frontal,occipital

In this paper we introduced a tool known as Sloreta to demonstrate the abnormalities between ASD and TD individuals.This is the first of its kind study to demonstrate the functional connectivity in patients with Sloreta. This paper proposes ERP as a biomarker for autism.The application of the results are helpful for functional localization which helps in diagnosis of this disorder at a early stage.Sloreta is a low cost software and is advanced version of LORETA. Sloreta can prove to be a good low resolution tool for early diagnosis of Autism spectrum disorder.

ERP is of high temporal resolution and is a established tool for diagnosis of nuerodevelopmental disorders.(Polich,2007) represented ERP as a valuable technique for assessing differences in individuals with ASD or ADHD. (Ducan et al 2009) investigated differences in ERP as a promising biomarkers for detection of Autism.

IV. CONCLUSION

The present paper proposed ERP based source localization based healthcare diagnostic system for assisting the doctors in decision making.This work has demonstrated Sloreta as a potential tool for ERP based source

localization.This paper suggested altered connectivity in individuals with ASD in the presence of visual stimuli.The suggested system can help to detect autism at a early stage.

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