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Gender Based Lateralization Effects on Resting State FMRI of ADHD Subjects

V. Solai Revathi, P. Udayaprasanth, S.P. Thaiyalnayaki and O. Uma Maheswari
Department of Electronics and Communication Engineering,
Digital Signal Processing Laboratory, College of Engineering,
Anna University, Guindy, 600025 Chennai, Tamil Nadu, India

Abstract: The bold signal obtained from fMRI (functional Magnetic resonance imaging) was decomposed into independent components using GIFT toolbox as suggested by Elena. The mean of the components across subjects , from which the Resting State Networks (RSNs) were identified for normal subjects and subjects with ADHD (Attention Deficit Hyperactivity Disorder) which is a condition described by inattention, hyperactivity and impulsivity. Lateralization whether Left or Right, identified using Laterality Cofactors (LCs). Comparison of the laterality cofactors between the healthy subjects and ADHD subjects was performed across the components. Lateralization for the ADHD subjects was more to the right compared to healthy subjects which had lateralization in both the left and right half.

Key words: Lateralization, laterality cofactors, fMRI, ADHD, resting

INTRODUCTION

Lateralization refers to the localization of activations in the human brain. Its effect on the two hemispheres of the brain was described by O. Agcaoglu. It is observed that the right part of the human body is controlled by the left hemisphere of the brain and vice versa. The left hemisphere is found to be involved with functions that are associated with language processing and logical and analytical thinking whereas the right hemisphere is associated with non verbal functions. Lateralization involves the amount of activations in either half of the brain or the domination of the left or right hemisphere for an associated function.

The resting state is defined as when the subject is not involved in any physical activity and is at rest. The rest state data proves very helpful in understanding the physical and mental conditions of persons affected with Schizophrenia, Alzheimer's condition and other mental disorders (Agcaoglu *et al*., 2015). When peak activations are observed in the left hemisphere of the brain, then that region of activation is said to be left lateralized and vice versa. The resting state fMRI data of the 16 healthy subjects and 25 ADHD subjects were analyzed as in and the lateralization of the RSNs was also obtained. Effects of gender on lateralization of brain networks (Agcaoglu *et al*., 2015) were also discussed and their effects on normal and ADHD subjects were also obtained.

Table 1: Demographic of subjects

No. of subjects	Male	Female	Age distribution	Mean age	SD
16 (Healthy)	8	8	20-40	28.6	5.7
25 (ADHD)	12	13	13-26	18.4	3.3

Participants: Data preprocessing and group ICA were performed using SPM and GIFT (Erhardt *et al*., 2011). Data was collected from NITRC. Data of the participants and their demographics are given in a Table 1. The data sets contain 16 healthy subjects and 25 ADHD subjects. The fMRI was taken under rest condition. The handedness of the subjects is not taken in to consideration (Erhardt *et al*., 2011).

MATERIALS AND METHODS

Preprocessing: Before working on the fMRI data, it was subjected to preprocessing. Preprocessing is necessary to correct for changes or orientations of the scans. Voluntary or involuntary head movements cause the slices to be disoriented. The data was preprocessed using an automated preprocessing tool SPM12 (Erhardt *et al*., 2011). The data was resliced to $3\times3\times3$ mm (Agcaoglu *et al*., 2015) voxels and realigned. The results are then spatially normalized to a standard MNI template that is provided with SPM and then smoothed using Full Width Half Maximum (FWHM) Gaussian kernel of 10 (Agcaoglu *et al*., 2015) to improve the signal to noise ratio of the data.

Corresponding Author: Solai Revathi, Department of Electronics and Communication Engineering,
Digital Signal Processing Laboratory, College of Engineering, Anna university, Guindy,
600025 Chennai, Tamil Nadu, India

Group independent component analysis: Group Independent component analysis decomposes BOLD into ICs by using GIFT 3.0 (Agcaoglu *et al*., 2015). Following preprocessing using SPM, intensity normalisation of the data was performed by dividing the time series of each voxel by its average intensity, converting data to percent signal change units (Erhardt *et al*., 2011). Using gICA (Calhoun *et al*., 2009) data were decomposed into functional networks. When applied to fMRI data, gICA identifies temporally-coherent networks by estimating maximally independent spatial sources or Spatial Maps (SMs), from their linearly-mixed fMRI signals or Time Courses (TCs) (Calhoun *et al*., 2001).

Using gift for Independent component analysis, single subject PCA (Principal Component Analysis) was performed for 100 components followed by group EM PCA for 75 components. Infomax algorithm was used for group Independent component analysis, extracting 75 components because it produced stable components (Calhoun *et al*., 2001) compared to other algorithms. ICASSO was run 20 times for stable results and Back reconstruction (Himberg *et al*., 2004) was performed using GICA.

RSN selection: Out of the 75 components for healthy controls, 20 components were identified as RSNs (Robinson *et al*., 2009). RSN identification (Erhardt *et al*., 2011) involved visually inspecting the Spatial Maps (SMs) and from the mean power spectra of the components across the subjects. One sample t tests of the components were performed and thresholded for one standard deviation and spatial maps were obtained.

Lateralization

Laterality maps: Lateralization was performed for subjects and based on gender. LUI tool (Swanson *et al*., 2011; Stevens *et al*., 2005) was used to obtain laterality maps. For each component, the difference between the intensity values on the left and its homotopic voxel (geometrically corresponding) (Agcaoglu *et al*., 2015) on the right hemispheres of the brain were taken. Spatial maps contain R~L differences on the right hemisphere and L~R differences on the left hemisphere. The laterality component B denotes the laterality for the components:

$$B = \begin{cases} R - L, \text{if } R > L \\ L - R, \text{if } L > R \end{cases}$$

Laterality cofactors: The measure of lateralization was done using Laterality Cofactors (LC) (Agcaoglu *et al*., 2015). It is defined as the ratio of difference between sum of intensities of the left and right hemisphere to the sum of intensities of the whole brain:

$$LC = \frac{\text{Sum of intensities on left} \sim \text{sum of intensities on right}}{\text{Sum of intensities of whole brain}}$$

RESULTS AND DISCUSSION

Healthy controls: The RSNs for this data are grouped into four regions; motor, auditory, DMN and frontal region. Out of the 75 components estimated 20 were found to be RSNs. The spatial maps of these RSNs are given below. The frontal network was found to contain 11 components, DMN contained 4 components, Auditory and motor contained 2 and 3 components respectively. The spatial maps corresponding to the RSNs of healthy subjects are given Fig. 1. The Talairach Table corresponding to the components is given in Table 2.

ADHD controls: 20 components were estimated out of which 7 were found to be RSNs. The RSN selection criteria was applied in the same way as previously. All of

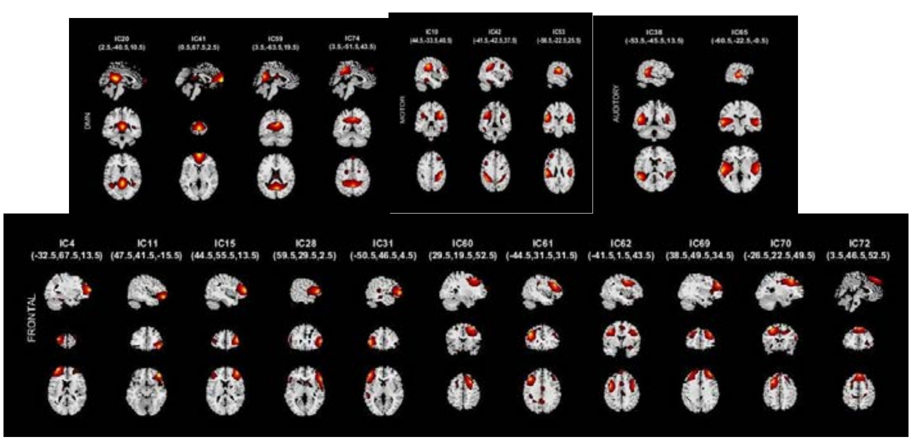

Fig. 1: Spatial maps of RSNs corresponding to: a) DMN; b) Motor network; c) Auditory network; d) Frontal network of healthy subjects

Table 2: Talairach table for RSNs of healthy subjects where BA denotes brodmann area

Component name	BA	Voxels per cluster	Coordinates(x, y, z) (mm, mm, mm)	t-statistic
IC 4				
Superior frontal gyrus	10	349	-30, 56, 17	29.33
uperior frontal gyrus	9	1	-21, 56, 26	9.21
IC 10				
Postcentral gyrus	2	493	48, -25, 32	26.91
IC 11				
Middle frontal gyrus	11	333	45, 44, -13	27.41
IC 15				
Middle frontal gyrus	10	385	42, 56, 8	24.07
IC 20				
Posterior cingulate	29	526	3, -37, 17	32.34
Medial frontal gyrus	10	7	0, 68, 2	5.34
IC 28				
Inferior frontal gyrus	45	386	51, 32, 2	24.01
IC 31				
Inferior frontal gyrus	10	452	-48, 50, 2	20.79
IC 38				
Sub-lobar, insula	13	384	-48, -37, 17	19.99
Superior temporal gyrus	41	26	51, -37, 14	15.48
IC 41				
Medial frontal gyrus	10	556	3, 65, 2	32.06
IC 42				
Supramarginal gyrus	40	362	-39, -40, 32	25.84
IC 53				
Inferior parietal lobule (L)	40	256	-54, -31, 28	20.82
Inferior parietal lobule (R)	40	154	57, -34, 22	17.47
IC 59				
Precuneus	31	630	3, -61, 23	36.2
IC 60				
Middle frontal gyrus	8	517	36, 23, 44	29.18
Sub-lobar, Insula	13	7	39, -46, 26	12.39
Sub-lobar, Insula	13	7	45, -40, 20	10.44
IC 61				
Middle frontal gyrus	46	375	-39, 38, 17	23.78
IC 62				
Middle frontal gyrus	6	212	-36, 5, 41	19.64
Precentral gyrus	6	53	45, 2, 35	12.21
IC 65				
Superior temporal gyrus (L)	22	556	-57, -22, 2	27.03
Superior temporal gyrus (R)	22	269	57, -22, 2	22.41
IC 69				
Superior frontal gyrus	9	288	33, 50, 26	19.88
Middle frontal gyrus	9	55	-33, 41, 29	12.01
IC 70				
Medial frontal gyrus	32	312	-18, 14, 41	22.26
Middle frontal gyrus	8	3	30, 32, 41	9.64
IC 72				
Superior frontal gyrus	8	322	3, 41, 53	30.78
Middle frontal gyrus	6	11	-36, 14, 47	10.5
IC 74				
Cingulate gyrus	31	614	-3, -46, 41	33.36

the components were in the frontal region only. The spatial maps of the RSNs are given below Fig. 2. The talairach table corresponding to ADHD subjects are given in Table 3.

Laterality cofactors

Healthy controls: The mean components were subjected to one sample t test across all the subjects and across male and female subjects for gender based laterality. The laterality cofactor values were calculated and plotted as a graph below in Fig. 3.

ADHD controls: In a similar procedure the laterality cofactor values were calculated for the ADHD controls after subjecting the components to one sample t test and was plotted as a graph as shown in Fig. 4.

From the laterality cofactors it was seen that certain components were lateralized to the left while certain components to the right. The component is said to be highly lateralized if it has laterality cofactor value >0.75 (Agcaoglu *et al*., 2015) and lateralized if laterality cofactor value is >0.2 (Agcaoglu *et al*., 2015). Any component value below 0.2 is not considered as lateralized.

Table 3: Talairach table for RSNs of ADHD subjects

Component name	BA	Voxels per cluster	Coordinates (x ,y, z) (mm, mm, mm)	t-statistic
IC 01				
Medial frontal gyrus	10	148	0, 65, 2	32.05
IC 10				
Superior frontal gyrus	10	209	36, 65, -4	25.07
IC 11				
Medial frontal gyrus	11	139	6, 62, -16	20.87
IC 15				
Medial frontal gyrus	11	38	0, 44, -13	17.63
IC 18				
Middle frontal gyrus	47	136	51, 53, -10	21.79
IC 19				
Anterior cingulate	32	231	0, 23, -7	29.34
IC 20				
Middle frontal gyrus	11	267	48, 50, -19	18.52

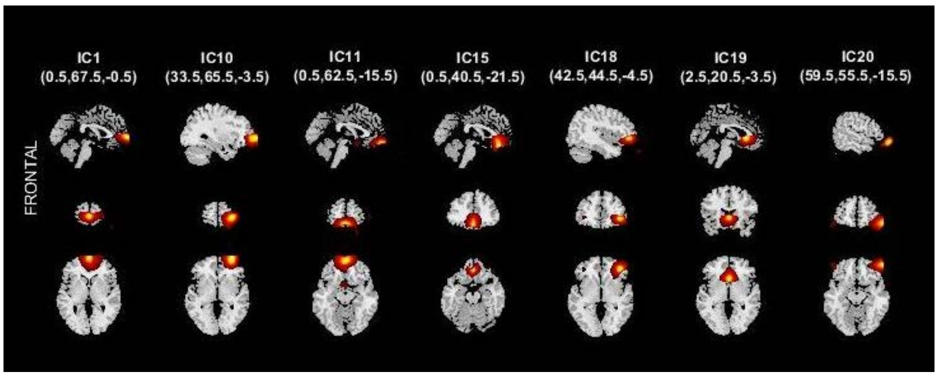

Fig. 2 : Spatial maps of RSNs corresponding to the frontal network of ADHD subjects

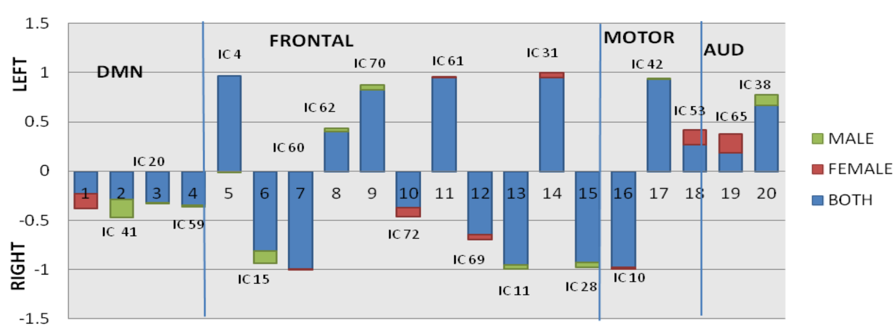

Fig. 3: Gender based laterality cofactors of healthy subjects

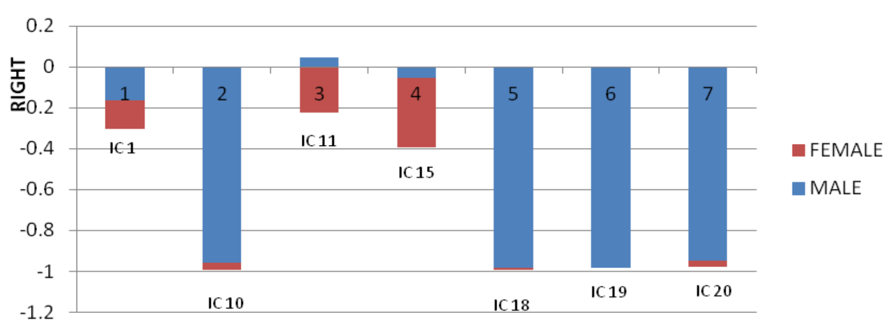

Fig. 4: Gender based laterality cofactors of ADHD subjects

In the case of healthy subjects it can be seen that most of the components of the DMN are lateralized to the right completely. And in that males have more lateralization than females. IC 41, 20 and 59 of the DMN are lateralized more for males than females and only IC 74 is lateralized more for females than males.

But in the case of frontal networks of the healthy subjects, components are lateralized in the left as well as in the right hemisphere of the brain. In this network, males and females have almost equal amount of lateralization in both the hemispheres, though males have slightly higher amount of lateralization. IC 51, 70, 11 and 28 are highly lateralized for males than females in either hemisphere. Whereas, independent components IC 60, 61 and 31 are highly lateralized for females than males.

CONCLUSION

Comparing for variations in the frontal network of both the subjects, taking this region of ADHD subjects it is seen that most of the components are lateralized to the right and females tend to have higher amount of lateralization than males. IC 10, 18, 20 are highly lateralized for females than males in the right part of the brain only. IC 10, 11, 15 have higher lateralization in females than males but the components have lesser amount of lateralization.

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