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Original Research Article

Brain networks and medical education

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ABSTRACT

Background: There has been significant progress in understanding the human brain with the development of modalities like functional magnetic resonance imaging (fMRI), positron emission tomography (PET) etc. Education is an important source of intellectual, emotional and cultural stimulus to the brain. In this resting fMRI study, we aim to map out specific regions in the brain in which changes occur relating to memory, language, motor, behavioural and cognitive functions after five years of undergraduate medical education and how this knowledge can bring us closer to understanding the brain and its functions and applications in clinical practice.
Methods: A total number of 48 normal, healthy medical students from our medical college were included in the study, and were divided into two groups, the first group completed five years of under-graduate medical training and the second group consisted of individuals who had only 4 months of exposure to medical training. Resting state fMRI study was performed and seed-to-voxel based functional connectivity analysis method was used to derive between group differences
Results: Out of the 48, 13 played one or more sport professionally, 8 were musically oriented with skills to play one or more musical instrument professionally and 9 had other talents (2-Good academic, 2-theatre, 3-dancing, 2-art like pottery and painting).
Conclusions: There were significant differences in the right inferior temporal gyrus which is the seat of many cognitive functions like language, emotion and memory and the left cerebellar hemisphere, which is known to play a role in fine motor functions, language and visual learning.

Keywords: Functional MRI, Resting state networks, Medical education, Cognition

INTRODUCTION

Many resting state fMRI studies have described the alteration in brain networks in conditions like depression, Alzheimer's disease, Multiple sclerosis, spatial neglect syndrome and seizures.[1-5] There is enough evidence to show that there have been significant changes in the fronto-parietal resting state networks with learning and education, however it is not the only network to be associated with learning as learning can be in various forms like visual, auditory and through practice etc.[6-8] Visual perceptual learning is said to modify the spontaneous activity in the brain.[9-10] Floyer-Lee et al showed that there is a significant increase in activation in the primary sensorimotor cortex contralateral to the hand which was trained in short and long term motor skill learning.[11] In another study conducted by Dehaene et al cortical networks of vision and language were shown to be significantly activated as children/adults learnt how to read.[12] In this resting fMRI study, we aim to map out specific regions in the brain in which changes occur after five years of undergraduate medical education and how this knowledge can bring us closer to understanding the brain and its functions.

METHODS

Sample selection

A total number of 48 normal, healthy medical students belonging to our medical college were included in the study and divided into two groups. The first group (Final year) consisted of 22 individuals who completed five years of under-graduate medical training. The second group consisted of 26 individuals who newly joined the course (First year) had only 3 months of exposure to medical training. The mean age of individuals of the first group was 24.75 (24-27) and the mean age of the second group was 17.8 (17-19). Male to female ratio was 1:1 in the first group and 0.8:1 in the second group. All the participants were admitted into the medical course on the basis of a common written entrance exam and an interview conducted by our institute and were residing in the hostels of the institution during the study. Study was approved by the Institutional Review Board and written informed consent was provided by all participants.

Acquisition

Data was acquired in a 3 Tesla MRI scanner (16 channels) in the department of radiodiagnosis. Anatomical study was acquired with a T1 MPRAGE (4 minutes) sequence with the following parameters: FOV-230 mm, slice thickness-0.9 mm and the number of slices per slab was 176, voxel size was 0.9×0.9×0.9 mm. fMRI was acquired with a spin echo EPI sequence using blood oxygen level dependent (BOLD) contrast with the following acquisition parameters: TR-2300 ms, TE-35 ms, FOV-230 mm, flip angle-90 degrees, slice thickness-4 mm, number of slices obtained was 34, voxel size was 3×3×3 mm and the matrix was 128×128 (8 minutes).

Pre-processing

MATLAB R2015b, along with SPM8 (Well come department of Cognitive neurology, London, UK) (www.fil.ion.ucl.ac.uk) was used for pre-processing. The steps were realignment, co-registration, normalization and smoothing. Five subjects (Two from group 1 and three from group 2) were excluded in this step as the translation motion exceeded 2 mm. The translation and rotation motion did not exceed±2 mm and 0.5 radians respectively in the rest of the 43 subjects. The motion differences were not statistically significant (t test, $p<0.01$) between the two groups. 3rd degree B spline interpolation with registration to the first image was used. The structural data was segmented for grey matter, white matter and CSF. The mean image after realignment was taken as source image. The smoothing at full-width half maximum (FWHM) was 8 mm.

fMRI connectivity analysis

CONN 16-b was used for the seed to voxel connectivity analysis. After feeding the basic details of the experimental set up, the Normalised anatomy and functional images were taken for the connectivity analysis to look at the regional differences between the two groups. The default AAL (Automatic anatomical labelling) atlas was used.[13] In the First level, the covariates of motion parameters were taken individually to all the subjects to do the cribbing and adjustment of the results. In the second level, covariates of the two individual experimental groups were taken to produce the connectivity values among them. The option was set to all the analysis condition. Denoising, first and second level analysis was completed using the same setup.

Statistical analysis

Voxel wise paired t-test analysis was done between the two groups to detect regions with significant differences. The between-subjects contrast of “final year>first year” was used. Whole brain cluster-level, false discovery rate (FDR) corrected threshold value of $p<0.001$ was used for the between-group statistical parameter maps which was more stringent than the normal $p<0.05$.

RESULTS

Demographic results

Out of the 48, 13 played one or more sport professionally, 8 were musically oriented with skills to play one or more musical instrument professionally and 9 had other talents (2-Good academic, 2-theatre, 3-dancing, 2-art like pottery and painting). Could these differences influence the networks and their interactions is something unknown! But these differences were not statistically significant (t test, $p<0.01$) between the two groups. Hence, they are not relevant to the study.

Differences in the resting state connectivity between the groups (final year>first year)

Our study showed significant differences in the resting state network connectivity between the two groups as hypothesized. Significant clusters with a minimum of 100 voxels are shown in Table 1 and the predominant areas showing differences are described below.

Right inferior temporal gyrus (posterior division) (MNI co-ordinates 50, -6, -38)

Group 1 had increased connections of the right inferior temporal gyrus with different brain regions as shown in Figure 1 A and B.

Right supplementary motor cortex (MNI co-ordinates, -6, -7, -61)

Group 1 had increased connections of the right supplementary motor cortex with different brain regions as shown in Figure 2 A and B.

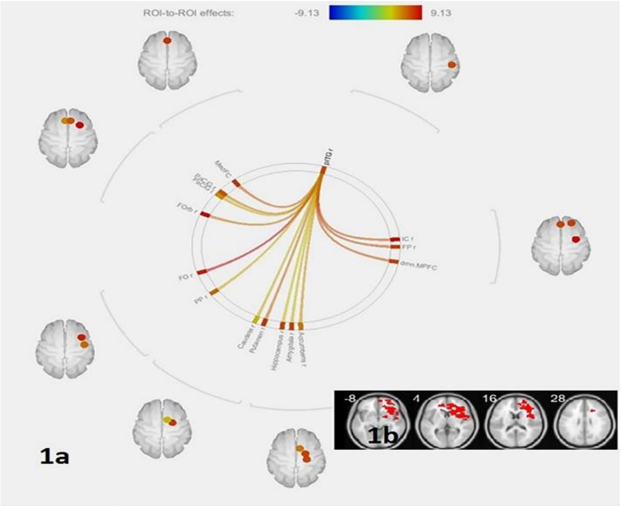

Figure 1 (a and b): Connectome ring of pITGr connections (final year>first year); Whole-brain-cluster-correlation maps of seed-to-voxel-based resting-state functional connectivity, final years>first years (FDR corrected p<0.001) with seed region in the right inferior temporal gyrus.

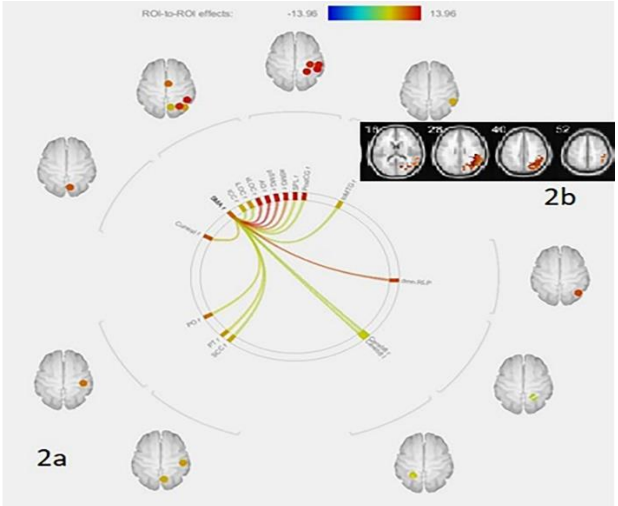

Figure 2 (a and b): Connectome ring of SMAr connections (final year>first year); Whole-brain-cluster-correlation maps of seed-to-voxel-based resting-state functional connectivity, final years>first years (FDR corrected p<0.001) with seed region in the right supplementary motor cortex.

Table 1: Seed-to-voxel-based connectivity results of only the significant clusters with more than 100 voxels (final year>first year).

Seed region	Connectivity region	Cluster size, p, (FDR corrected)	Cluster size (No. of voxels)	Beta value	T value	MNI co-ordinates (x, y, z)
Right inferior temporal gyrus (posterior division) (All increased connections) (50, -6, -38)	Right frontal pole	0.00001	906	0.76	3.91	(-34,46,20)
	Frontal medial cortex		195	0.57	2.31	(-27,63,3)
	Right frontal operculum cortex		233	0.9	4.13	(-60,15,27)
	Right putamen		194	0.73	2.9	(30, -3,3)
	Right caudate		143	0.37	2.33	(10, 22, -2)
	Cingulate gyrus (anterior division)		123	0.16	0.66	(3, 29, -5)
	Right temporal pole		118	0.78	2.1	(50, 6, -18)
	Right insular cortex		422	0.82	3.11	(40, -28, 20)
	Right frontal orbital cortex		413	0.8	2.78	(16, 8, -10)
	Right central opercular cortex		257	0.59	2.1	(45, -28, 22)
	Right paracingulate gyrus		210	0.57	2.43	(2, 22, -2)
Right supplementary motor cortex (Increased connections), (-6, -7, -61)	Right angular gyrus	0.000001	750	0.9	3.58	(-40, 52, 38)
	Right supra-marginal gyrus (posterior division)		420	0.84	2.91	(47, -54, 20)
	Pre-cuneous cortex		198	0.38	1.19	(4, -68, 32)
	Right lateral occipital cortex (superior division)		1965	0.73	3.07	(-46, 68, 4)
	Right cuneal cortex		195	0.75	2.85	(18, -75, 20)
Left cerebellum (Increased connections), (-46, -52, -40)	Right supplementary motor cortex	0.00001	233	0.63	3.65	(26, -3, 47)
	Cingulate gyrus (Anterior division)		223	0.34	1.95	(3, 29, -5)
	Left supplementary motor cortex		150	0.53	3.71	(-4, -4, 60)
	Right paracingulate gyrus		257	0.29	1.7	(2, 22, -2)
Left cerebellum (Decreased connections), (-46, -52, -40)	Left angular gyrus	0.00001	342	-0.58	-3.19	(-40, -64, 45)
	Left supramarginal gyrus (posterior division)		124	-0.44	-2.79	(-54, -43, 19)
	Left lateral occipital cortex (Superior division)		1478	-0.61	-3.11	(-48, -76, 6)

Left cerebellum (region 9) (MNI coordinates, -46, -52, -40)

Group 1 had increased connections of the left cerebellum with different brain regions, shown in Figure 3 A and B.

Group 1 had decreased connections of the left cerebellum with different brain regions, shown in Figure 4 A and B.

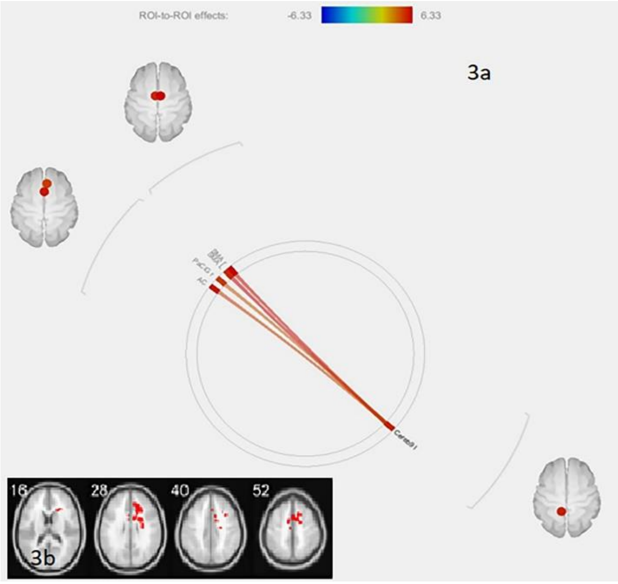

Figure 3 (a and b): Connectome ring of cerebellar increased connections (final year>first year); Whole-brain-cluster-correlation maps of seed-to-voxel-based resting state functional connectivity, final years>first years (FDR corrected p<0.001) with seed region in the left cerebellum.

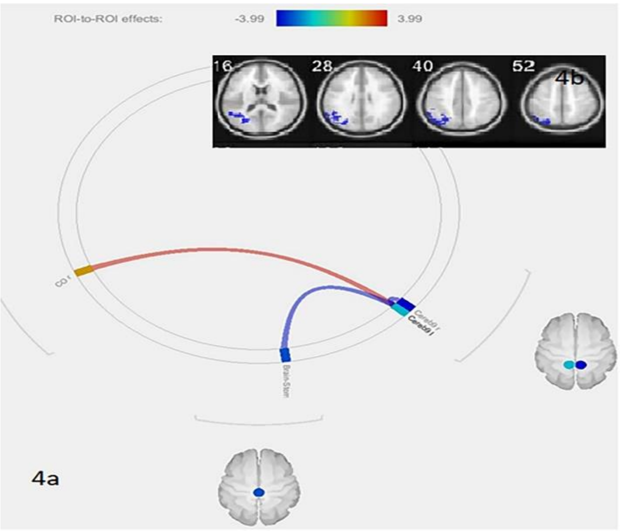

Figure 4 (a and b): Connectome ring of decreased connections of the left cerebellum (final year>first year); Whole-brain-cluster-correlation maps of seed-to-voxel-based resting-state functional connectivity, final years>first years (FDR corrected p<0.001) with seed region in the left cerebellum.

DISCUSSION

From the results, it is clear that the groups were adequately matched in the demographic variables except in the number of years of medical training. Hence, we attribute these changes to be brought by the impact of medical education. The changes seen were mainly localized to the right temporal lobe, right supplementary motor cortex and left cerebellar hemisphere.

Temporal lobe and its interactions

Temporal lobe of the brain is known to be predominantly affected in patients with semantic dementia, in which patients show cognitive decline of predominantly conceptual database and underlying language, thus increasing the validity of the importance of the temporal lobe in cognitive functions.[14,15] In our study, there were increased connections of the right inferior temporal gyrus with areas of the frontal cortex such as frontal orbital cortex, frontal and central opercular cortex, cingulate and paracingulate cortex. The increase in the temporal lobe connectivity could be related to the understanding of new concepts, whether in relation to concepts about diagnosing or treatment. The temporal lobe also plays an important role in skills related to language. Medical training in a national tertiary institution involves dealing and interacting with patients from all over the country and people of different languages. The development of better networks in regions associated with language is thus a good sign. Bilateral temporal lobectomy in female rhesus monkeys led to symptoms like psychic blindness (visual agnosia) and profound emotional disturbances suggesting that the temporal lobe may have a role to play in emotions and visual processing.[16] The development of empathy while dealing with patients involves a combination of foresight and insight and depends on evolution of structures of the brain associated with vision.[17] The medial temporal lobe, involving the hippocampus, amygdala and the surrounding cortices are seen to interact with the prefrontal cortex (anterior and lateral predominantly), which is responsible for recall and processing of information into memory.[18,19] They act together during the process of encoding and storing information into long term memory and retrieval during a task, thus showing that brain regions do not act independently but form networks across regions to perform certain functions and this interaction is important for memory encoding and retrieval which is a very important component of medical education.

Few studies have shown the integration of different networks involving the parietal cortex and inferior temporal cortex in task learning.[20] The right hemisphere which in our study showed an increase in networks after medical education is shown to play an important role in object location memory, and retrieval of this information from memory.[21-23] There is no denying the fact that object location memory is very important for a doctor in training especially in the aspects of the human body anatomy.

Supplementary motor cortex and its interactions

Previously named as a "supplement" to the motor cortex, in recent times with the advance of brain imaging methods, the supplementary motor cortex is now thought to be more of a requirement than a supplement.[24] Electrical stimulation of the right supplementary motor cortex showed stimulation of sensations such as the "urge" to perform a certain action and evoked motor functions ipsilaterally and bilaterally.[25] Through mediation of the primary motor cortex and the medial limbic cortex, it is said to be crucial in programming, elaboration and fluent execution of an action sequence.[26] This suggests that the supplementary motor cortex is involved in the thought control of an action and has left-right specialization. Along with the basal ganglia it has been implicated in memory encoding and retrieval.[27] Anatomically it forms a part of the dorso-medial frontal cortex which shows increased activity in relation to adaptive goal-directed behaviour.[28] This kind of behaviour plays a major role in cognitive control and also seen while individual becomes more mature.

Cerebellum and its interactions

Though not studied in detail as compared to the cortical regions, studies have shown the importance of cerebellum in many motors, language and cognitive functions.[29] It is said to be associated with the learning of higher and fine motor functions, which could be related to learning new procedures or related to excessive writing in medical training.[30] Our study showed increased activity in the region of the left cerebellar hemisphere. Structural changes of the cerebellum developing over the course of evolution are thought to be a pre requisite for the development of human language.[31] Structurally, the lateral part is involved in language, planning and thought modulations.[32] The cerebellum is connected to the frontal cortex through the pons, thalamus, para-hippocampal structures and the cingulate gyrus.[34] Our study showed increased connections with the supplementary cortex, cingulate and paracingulate cortex after 5 years of medical training, which are responsible for performance of higher functions and complex behaviours.[35]

Our study also showed reduced connections between the left cerebellum with the ipsilateral parietal (angular and supra marginal gyrus) and occipital lobes and contralateral cerebellum in the final year compared to the first-year students which could be reflective of suppression or pruning of these connections because of the increased cortical control. Pruning of existing connections with the development of cognitive control is a well-known phenomenon in adolescence and absence of normal pruning has been implicated in several diseases like alcoholism, autism etc.

Cingulate cortex and its interactions

In our study the cingulate gyrus (anterior division) has been seen consistently in the regions showing increased activity (the right inferior temporal gyrus and the left cerebellum) in the group with five years of medical training. Studies have shown that the increased interaction of the anterior cingulate cortex with other distant regions in the frontal, temporal and parietal lobes is one of the important underlying mechanisms of education related brain reserve seen in healthy adults.[36] The same study showed that increased connections of the anterior cingulate cortex with the hippocampus, posterior cingulate gyrus, angular gyrus and inferior frontal lobe were related to better cognitive performances. The anterior cingulate cortex is different from the other fronto-cortical regions due to its involvement in multiple functions and functional overlap.[37] Dense projections to the motor cortex and spinal cord raise the possibility of involvement in various motor functions. Afferents from the thalamus and brain stem suggest its importance in the arousal/drive state of the brain.

Limitations

We looked at changes in resting state networks. From previous research, resting state networks have been shown to be consistent in the temporal, spatial and frequency parameters among different individuals. However, the current study indicated more activation in the temporal regions secondary to higher medical education. A task-based fMRI study could have been more evident to assess the networks and cognitive abilities, as previously studied by authors. Although there was no significant difference in the demographic data and the intellectual level as they cleared a similar pattern of entrance exam and interview procedure, a separate neuropsychology evaluation would have revealed a better understanding on the individual differences.

CONCLUSION

Our study showed significant differences in the resting state networks in a group of individuals who had more exposure (5 years) in medical training as compared to the other group who had very less medical training exposure (3 months). These changes were mainly located in the right inferior temporal gyrus and frontal lobes which is the seat of many cognitive functions like language, emotion and memory and changes seen in the left cerebellar and cortical interactions are known for the motor functions, language, visual learning including cognitive parse. Our results are in line with results of previous research on effect of education/different educational methods on the brain networks. Also, studies have shown that years of education has influence in connectivity related working memory. In conclusion, our study reveals the idea of the effect of medical education or education in normal brain networks which provides us a better understanding of the brain behaviour and connectivity patterns. This knowledge can be applicable in understanding brain abnormalities in various cognitive disabilities or disorders and can aid us in treatment and rehabilitation.

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Ethical approval: The study was approved by the institutional ethics committee

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