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Artikel Asli/*Original Article*

Resting State Effective Connectivity between Inferior Parietal Lobe (IPL) and Inferior Temporal Gyrus (ITG) in the Left and Right Hemispheres

(Kehubungan Berkesan Keadaan Rehat antara Lobus Parietal Inferior (IPL) dan Girus Temporal Inferior (ITG) dalam Hemisfera Kiri dan Kanan)

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ABSTRACT

Inferior parietal lobule (IPL) and inferior temporal gyrus (ITG) are two important brain regions for the default mode network (DMN). IPL has been known to be involved in the control of attention and responding to given information while ITG is involved in the processing and perception awakened by visual stimuli. These two key DMN regions are highly interconnected as determined from white matter and fiber tracking studies. However, little is known about their nature of connectivity while the brain is at rest, whether it is linear, bilinear or nonlinear and whether it is of mono- or bi-direction. Resting state functional magnetic resonance imaging (rsfMRI) data were obtained from 7 healthy male and female participants (average age = 20.7 ± 4.5 years) and were concatenated. Data were analyzed using statistical parametric mapping (SPM12). Endogenous brain signals were modelled by Fourier series at 0.01 – 0.08 Hz. IPL-ITG connected linear, bilinear and non-linear causal models in both hemispheres were constructed and estimated by means of stochastic dynamic causal modelling (sDCM) and were compared using Bayesian Model Selection (BMS) for group studies. Group fixed-effects results indicated that bilateral IPL and ITG exhibited high neural activity at a corrected significant level ($p_{FWE} < 0.05$). Neural activity was centered in ITG (-32/2/-38) in the left hemisphere but shifted to IPL (32/-38/50) in the right hemisphere indicating different control center for both hemispheres. BMS selected bilinear model as the optimal model for both hemispheres (model posterior probability ~ 1.0; log evidence > 1000) which has the best balance between model accuracy and difficulty. The minimum free energy (F) = -4.41×10^4 and -4.09×10^4 for left and right hemisphere bilinear models respectively. From BMS and DCM results, it was found that IPL and ITG do have a dynamic collaboration between each other, a connectivity that belongs to a greater network when the brain is at rest. The intrinsic connections between them are negative in both directions i.e. IPL and ITG mutually inhibited each other. The effective connectivity was modulated by the endogenous fluctuation of the brain signal.

Keywords: Resting state; Bayesian; winning model; causal; stochastic DCM (sDCM)

ABSTRAK

Lobus parietal inferior (IPL) dan girus temporal inferior (ITG) ialah dua kawasan penting otak bagi rangkaian mod lalai (DMN). IPL telah diketahui terlibat dalam mengawal perhatian dan bertindak balas terhadap maklumat yang diberi manakala ITG terlibat dalam pemprosesan tanggapan yang dibangkitkan oleh stimulus penglihatan. Dua kawasan utama DMN ini saling berhubungan seperti yang terbukti daripada kajian jirim putih dan laluan gentian. Walau bagaimanapun, masih sedikit diketahui mengenai kehubungan sesama mereka semasa otak sedang berehat, sama ada linear atau tak linear dan sama ada bersifat satu atau dua arah. Data pengimejan resonans magnet kefungsian keadaan rehat (rsfMRI) diperolehi daripada 7 orang peserta lelaki dan wanita (purata umur = 20.7 ± 4.5 tahun) yang dijeraitkan. Data dianalisis menggunakan pemetaan statistik berparameter (SPM12). Isyarat endogen otak dimodel menggunakan siri Fourier pada 0.01 – 0.08 Hz. Model linear, bilinear dan tak linear yang menghubungkan IPL-ITG dalam kedua-dua hemisfera dibina dan dianggar menggunakan pemodelan sebab dan akibat dinamik stokastik (sDCM) dan dibanding menggunakan pemilihan model Bayesian untuk kajian berkumpulan. Keputusan kesan malar berkumpulan menunjukkan bahawa IPL dan ITG bilateral memperlihatkan pengaktifan neuron yang tinggi pada aras keertian diperbetulkan. Aktiviti neuron berpusat di ITG (-32/2/-38) dalam hemisfera kiri tetapi beranjak ke IPL (32/-38/50) dalam hemisfera kanan menunjukkan pusat kawalan berbeza dalam kedua-dua hemisfera. BMS memilih model bilinear sebagai model optimum untuk kedua-dua hemisfera (kebarangkalian model posterior ~ 1.0; log pembuktian > 1000) yang memiliki keseimbangan terbaik antara ketepatan dan kesukaran model. Tenaga bebas minimum (F) = -4.41×10^4 dan -4.09×10^4 masing-masing untuk model bilinear hemisfera kiri dan kanan. Daripada keputusan BMS dan DCM, didapati bahawa IPL dan ITG mempunyai kolaborasi dinamik antara satu sama lain; kehubungan yang dimiliki oleh suatu rangkaian yang lebih besar semasa otak berehat.

Kehubungan intrinsik di antara mereka adalah negatif dalam kedua-dua arah iaitu IPL dan ITG saling merencat antara satu sama lain. Kehubungan efektif dipinda oleh turun naik endogenus isyarat otak.

Kata kunci: Keadaan rehat; Bayesian; model pemenang; sebab dan akibat; DCM stokastik (sDCM)

INTRODUCTION

The default mode network (DMN) is part of the brain functional structure that shows a significant increase in neuronal activity and energy consumption as compared to other brain regions when the brain is at rest (Raichle et al. 2001; Raichle & Snyder 2007). DMN comprises of several brain regions such as posterior cingulate cortex (or precuneus) (PCC), middle prefrontal cortex (MPFC), inferior parietal lobule (IPL) and inferior temporal gyrus (ITG) (Di & Biswal 2014). These main areas in the brain forming DMN, also known as nodes, are connected to each other as indicated by the studies on the brain white matter fiber nerves (Greicius et al. 2009; van den Heuvel et al. 2008; van den Heuvel et al. 2009) and the synchronization of functional magnetic resonance imaging (fMRI) signal (Biswal et al. 2010; Greicius et al. 2003).

DMN is not just being activated in a state of resting but has also been found to be activated during task-based spontaneous cognitive activity (Andrews-Hanna et al. 2010), motor function (Yusoff 2013) working memory retrieval, emotion and social cognitive (Laird et al. 2011; Smith et al. 2009; Spreng et al. 2009). However, the DMN nodes are functionally heterogenous in nature with each node has different functional specialization (Laird et al. 2009). This specialized function of each node is not completely understood. Furthermore, in the context of functional specialization and functional integration, the specific function of an area in the brain can only be fully understood by knowing the connectivity between any particular areas with other areas in the brain (Friston 2011). Study on how this flow of information (effective connectivity) occurs among DMN nodes is possible via dynamic causal modeling (DCM) (Di & Biswal 2014).

Inferior parietal lobule (IPL) also known as Brodmann Area (BA) 40 and inferior temporal gyrus (ITG), BA37, are two important brain regions of the default mode network (DMN). IPL has been known to be involved in the control of attention and giving feedback to received information while ITG is involved in the processing the perception created by visual stimuli. These two neural sites have also been found to be responsible to visual context processing such as colors, shapes and objects, together with the inferior frontal gyrus (IFG) and postcentral gyrus (PG) (Kwon et al. 2016; Wu et al. 2017).

Despite numerous findings about the behavior of ITG and IPL when the visual- and attention-related tasks are given to the participants, the questions of whether the two regions will also actively take part in the absence of tasks are still being investigated. Moreover, little is known about the nature of connectivity between these two DMN regions while the brain is at rest, whether it is linear, bilinear or nonlinear and whether it is of mono- or bi-direction. If the connectivity between the two regions is significant in which ever form it might be, a complete understanding about the existing network connecting the two regions is vital because they have important roles in both active and rest conditions.

Among the many aims of resting state fMRI (rsfMRI) is to determine the DMN and the effective connectivity that exists while the brain is at rest. “Brain at rest” means that neither sensory nor contextual stimulus will be used to evoke brain activation. Participant is not required to perform any task but to lay still with eyes on a fixation point. Participants were also told not to be in the state of “day dreaming” or “mind wandering”. Thus, commonly used model-based statistical parametric mapping (SPM) is best coupled with independent component analysis (ICA) (Calhoun et al. 2001) to determine brain activation. In order to model brain responses in the absence of exogenous inputs, low frequency fluctuation (LFF) that can be computationally generated by Fourier sinusoidal function of different oscillating frequencies (Androulidakis et al. 2008) can be used as native or endogenous input, originating or occurring naturally inside the brain. LFF was assumed to occur within the brain when it is at rest (Di & Biswal 2014) rendering modelling possible using Fourier sinusoidal function.

In this work, Statistical Parametric Mapping (SPM), DCM and ICA via Group ICA for fMRI Toolbox (GIFT) (Calhoun et al. 2001) were used to investigate the effective connectivity between two important DMN regions – IPL and ITG – in the right and left hemispheres of the brain. The rsfMRI data obtained from 7 healthy participants were concatenated and were analyzed using mass univariate analysis of SPM to obtain significant activation.

The effective connectivity between the two regions was accomplished via a multivariate analysis of stochastic DCM. It is hypothesized that the low amplitude LFF signals that exist within the DMN nodes, in particular the IPL and ITG, when the brain is at rest can be modelled and would be able to represent the neuronal activity. In modeling the effective connectivity, the LFF is hypothesized to exert an influence onto a node as an endogenous input and modulate the effective connectivity that exists between the nodes.

The present rsfMRI study rests on three main objectives; (1) to determine whether ITG and IPL are significantly activated when the brain is at rest, (2) to determine the effective connectivity among those two areas when the brain is at rest via causal modelling and (3) to determine the optimum model among linear, bilinear and non-linear models that has the best balance between model difficulty and model accuracy, that would be able to explain the possible connectivity between ITG and IPL.

In relation to the brain behavior, the output obtained from modeling the connectivity between ITG and IPL is very useful for the determination of the brain symmetrical behavior. Similar connectivity models between ITG and IPL in both hemispheres may indicate symmetrical characteristics of the brain in that particular region during resting state.

Moreover, the successful parameterization of the optimum resting state connectivity model will show that the endogenous LFF does really occur inside the brain when the brain is at rest which can be further studied and explored.

Furthermore, from the information about linearity and directionality of a model that can be obtained from causal modeling, one will be able to determine any particular region that is more influential than the others.

EXPERIMENTAL METHODS

SUBJECTS

This study is a pilot study and the scope of this study represents parts of a parent study. Seven healthy male and female participants (average age ± standard deviation = 20.7 ± 4.5), were conveniently recruited for this study. The participants agreed to participate by filling in the informed consent and screening forms and signing them, after being given full explanation of the nature and risks of the research. This study has been approved by the institutional ethics committee (IEC) UKM PPI/111/8/JEP-2016-307. All participants reported no history of psychiatric or neurological disorder and no current use of any psychoactive medications.

fMRI SCANS

The rsfMRI BOLD imaging protocol was executed using Siemens Magnetom Verio 3T at Universiti Kebangsaan Malaysia Medical Centre (UKMMC). The first two scans were dummies and were automatically discarded by the BOLD imaging protocol to eliminate the magnetic saturation effect. The gradient echo-echo planar imaging (GRE-EPI) parameters for acquiring functional T2* weighted images are echo time (TE) = 29 ms, repetition time (TR) = 2 s, flip angle (α) = 75°, slice thickness = 3.5 mm, slice gap = 1.05 mm, field of view (FOV) = 240 mm, matrix size = 64 × 64, voxel size = 3.75 × 3.75 × 4.55 mm, number of scans = 200 and total imaging time = 9 minutes 33 s (Abbott et al. 2013).

The participants were told not to move their head during the scan and were instructed to empty their mind and to passively focused on a fixation point "x" symbol throughout the session. Participants must not fall asleep during the scan because "sleeping brain" is very much different to "resting brain" (Yeo et al. 2015). Participants were also told not to be in the state of "day dreaming" or "mind wandering" throughout the scanning session. The state of consciousness of the participants throughout the scan was verified after the scan completed.

PRE-PROCESSING

The T2*-weighted rsfMRI data were analyzed using MATLAB 7.10.0 (R2010a) (Mathworks Inc. MA, USA) and Statistical Parametric Mapping (Functional Imaging Laboratory (FIL), the Wellcome Trust Centre for NeuroImaging (WTCN), in the Institute of Neurology at University College London (UCL), UK.) version 12 (SPM12) (www.fil.ion.ucl.ac.uk/spm/). Functional images in each measurement were realigned using the 6-parameter affine transformation in translational (x, y and z) and rotational (pitch, roll and yaw) directions to reduce artifacts from participant's movements. After realigning the data, a mean image of the series is used to estimate some warping parameters that map it onto a template that already conforms to a standard anatomical space (EPI template provided by the Montreal Neurological Institute-MNI). The normalization procedure used a 12-parameter affine transformation. The images were then smoothed using an 8-mm full-width-at-half-maximum (FWHM) Gaussian kernel. Low-frequency responses caused by aliased biorhythms, cardiac effects and other oscillatory signal variations were removed using high-passed filter.

GENERAL LINEAR MODEL

Human brain has been found to exhibit low frequency signal (LFF) when it is at rest. This LFF ranges from 0.01 to 0.08 Hz (Cordes et al. 2001). The LFF detected during resting state is associated with internally and externally oriented consciousness (Vanhaudenhuyse et al. 2011). Thus, to model the LFF, a combination of mathematical functions such as sine and cosine functions of different frequencies that show a resemblance of LFF, can be used. The functions, also known as Fourier basis set (Glaser & Friston 2004), can be incorporated into the general linear model (GLM) as shown by the design matrix in Figure 1. This Fourier basis set with $N_s = 4$ is thought to be suitable to model brain responses during resting state which is assumed to oscillate between 0.01 – 0.08 Hz (Di & Biswal 2014).

In Figure 1, columns 1 to 8, denoted as parameters, represent the Fourier basis set with 90° phase delay oscillating at 0.01 Hz (column 1 & 2), 0.02 Hz (column 3 & 4), 0.04 Hz (column 5 & 6) and 0.08 Hz (column 7 & 8) (Di & Biswal 2014). Column 9 represents the effects that may be caused by other factors. On the other hand, horizontal lines in the design matrix, denoted as images, are number of scans. In this study, the 200 rsfMRI functional scans for each of the seven participants were concatenated to produce a single design matrix with 1400 scans or measurements. The GLM shown in Figure 1 was then estimated. By using a MATLAB-based WFU Pick Atlas toolbox (Wake Forest University, North Carolina, USA), significant activations for

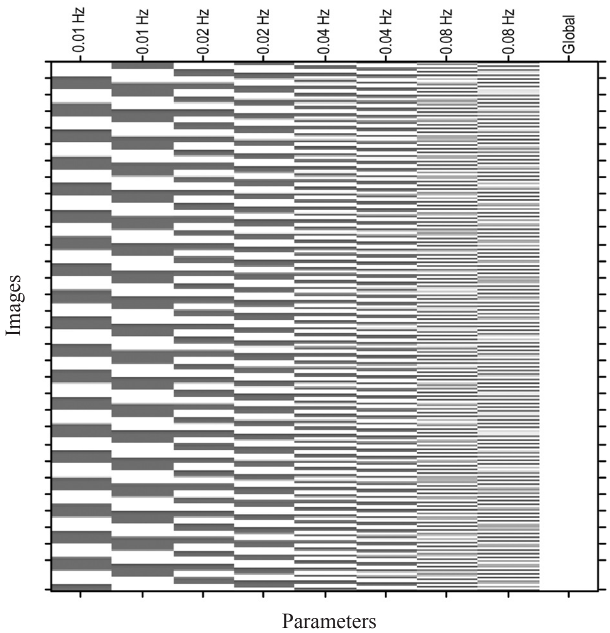


FIGURE 1. Design matrix for the GLM used in this study as explained in the text for the left and right hemispheres

IPL and ITG in the left and right hemispheres were obtained and their statistics and maximum intensity coordinates were recorded. This was done at $p < 0.05$, corrected for multiple comparisons, based on the whole brain activation due to the effects of interest using *F*-contrast.

INDEPENDENT COMPONENT ANALYSIS

The Group Independent Component Analysis (ICA) of fMRI Toolbox (GIFT) (http://icatb.sourceforge.net/) (Calhoun et al. 2001) was used determine the existence of any independent components (IC) within the average resting brain of all participants. Five components were extracted and the resulting component maps were visually inspected to identify the bilateral ITG and IPL. The results were compared with that obtained from SPM analyses for confirmation.

DYNAMIC CAUSAL MODELLING

The effective connectivity among the regions of interest (ROIs) was studied using dynamic causal modelling (DCM12) (www.fil.ion.ucl.ac.uk/spm/). Using the maximum intensity coordinates of the brain activation in the left and right hemisphere IPL and ITG as the center of each ROI (defined as a sphere of 5-mm radius), four linear, bilinear and non-linear causal models were constructed (Figure 2), from which the time series response was extracted (Stephan et al. 2010). The model was then inverted and inferred using DCM12. In Figure 2, all models are assumed to have a bidirectional connection between IPL and ITG; as the ROIs (Dark arrows). This connection is triggered by the endogenous LFF input (Bold arrows) into the ROIs. This input is not exogenous but endogenous LFF as represented by the Fourier basis set mentioned above. Figure 2(a) is a linear model. In a bilinear model (Figure 2(b)), the connection is modulated by the LFF (Dashed line). In a non-linear model (Figure 2(c and d)), the effective connectivity between the ROIs is not modulated by the LFF but is gated (Curved arrow) by the activity in the region itself.

The models for each hemisphere were then compared using Bayesian Model Selection (BMS) method for group studies under FFX framework (Stephan et al. 2009). This is done in order to obtain an optimal model that would be able to explain the data. The optimum model is the model that has the best balance between accuracy (fit) and difficulty.

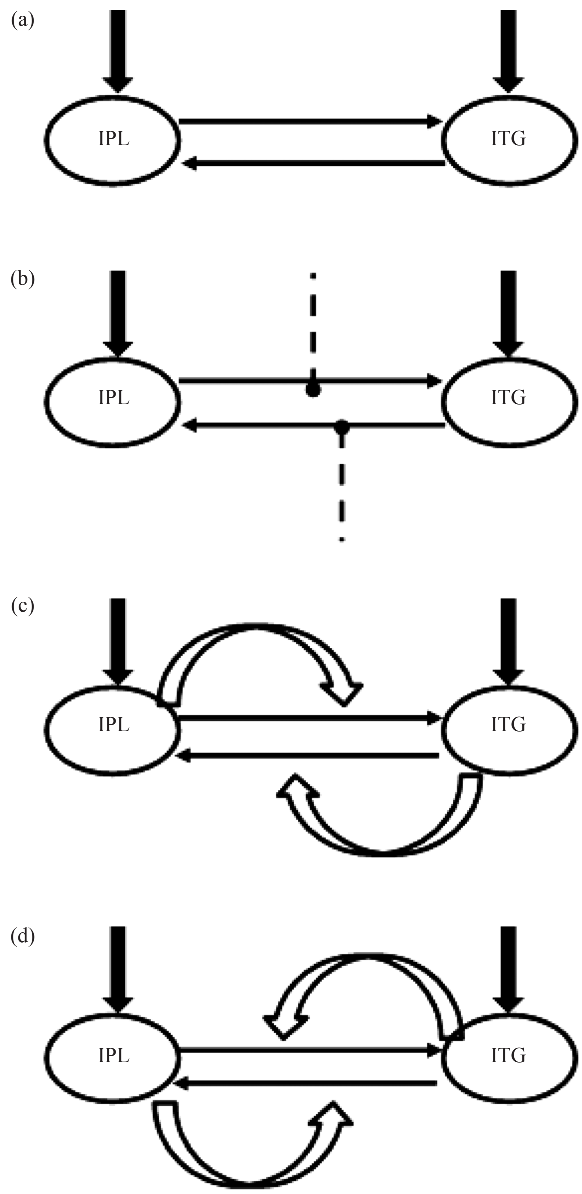


FIGURE 2. Dynamic causal models proposed for this study

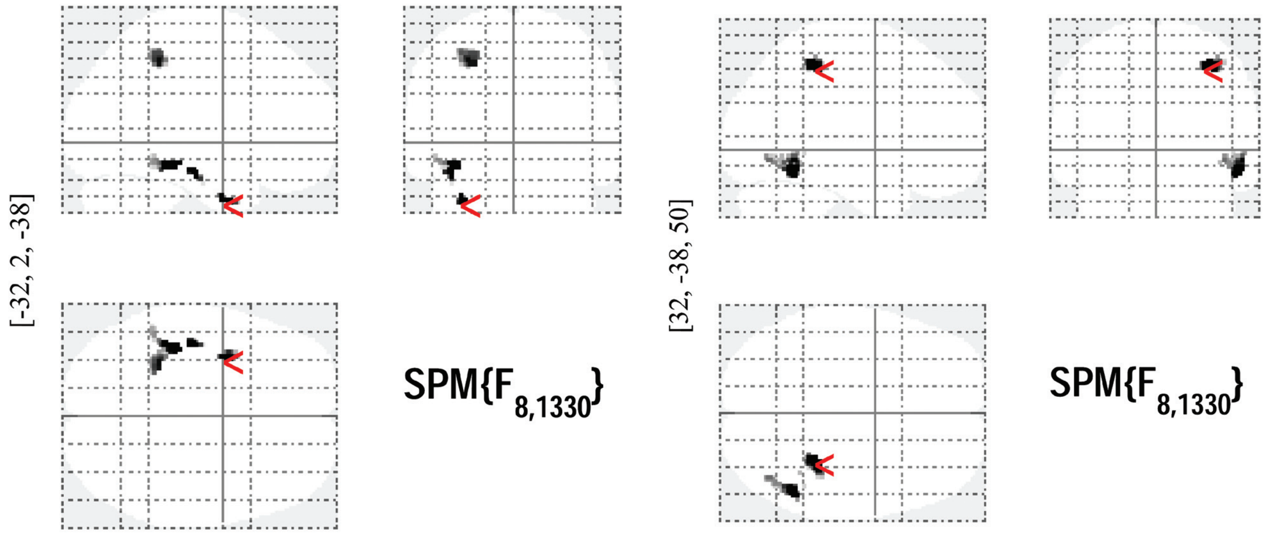


FIGURE 3. Significant ($p < 0.05$) group activation in IPL and ITG in the left (left) and right (right) hemisphere obtained from seven participants

RESULTS

BRAIN ACTIVATION

Figure 3 shows the maximum intensity projection (MIP) in the left (left) and right (right) hemisphere for IPL and ITG when the brain is at rest. The results were obtained from fixed-effects analysis (FFX) performed on concatenated data of the seven participants. The arrow head (<) indicates the point of maximum intensity with the Montreal Neurological Institute (MNI) coordinates (x, y and z) shown on the left side of the figure. The coordinates of maximum intensity is in ITG in the left hemisphere but changes to IPL in the right hemisphere. Details about the activation statistics for the respective regions obtained from SPM and WFU Pickatlas (Automatic Anatomical Labelling – AAL) are given in Table 1 and Table 2. The tables show that both left and right hemisphere IPL and ITG clusters are significantly activated ($p < 0.05$, corrected for multiple comparisons) when inferred at set and cluster levels. There are more clusters of activation in the left as compared to in the right hemispheres. In Addition, all voxels containing a cluster are significantly activated at peak level.

TABLE 1. Activation characteristics for right hemisphere ROIS

	Right hemisphere	
AAL	IPL	ITG
Set-level		
p	< 0.05	
C	2	
Cluster-level		
p	< 0.05	< 0.05
k_E	56	62
Peak-level		
p	< 0.05	< 0.05
F	6.28	6.18
z	5.31	5.25
MNI coordinates		
x	32	50
y	-38	-56
z	50	16

C = number of significantly activated cluster; k_E = number of significantly activated voxels; *F, z = statistics*

TABLE 2. Activation characteristics for left hemisphere ROIS

	Left hemisphere			
AAL	ITG	ITG	ITG	IPL
Set-level				
p		< 0.05		
c		4		
Cluster-level				
p	<0.	<0.05	<0.0	<0.0
k_E	05	14	5	5
	21		33	63
Peak-level				
p	<0.	<0.05	<0.0	<0.0
F	05	7.08	5	5
z	7.1	5.79	6.44	5.85
	3		5.41	5.05
	5.8			
	2			
MNI Coordinates				
x	-32	-40	-40	-30
y	2	-22	-30	-42
z	-38	-18	-14	48

C = number of activated significantly cluster; k_E = number of significantly activated voxels; *F, Z = statistics*

ICA RESULTS

Figure 4(a) shows GIFT results indicating five independent components (ICs) which include activated areas in the frontal, temporal, occipital and parietal regions. The IPL and ITG are among the five ICs that are significantly activated see Figure 4(b). The results are in accordance with that obtained from the present SPM analysis and in consistent with previous findings (Di & Biswal 2014).

EFFECTIVE CONNECTIVITY

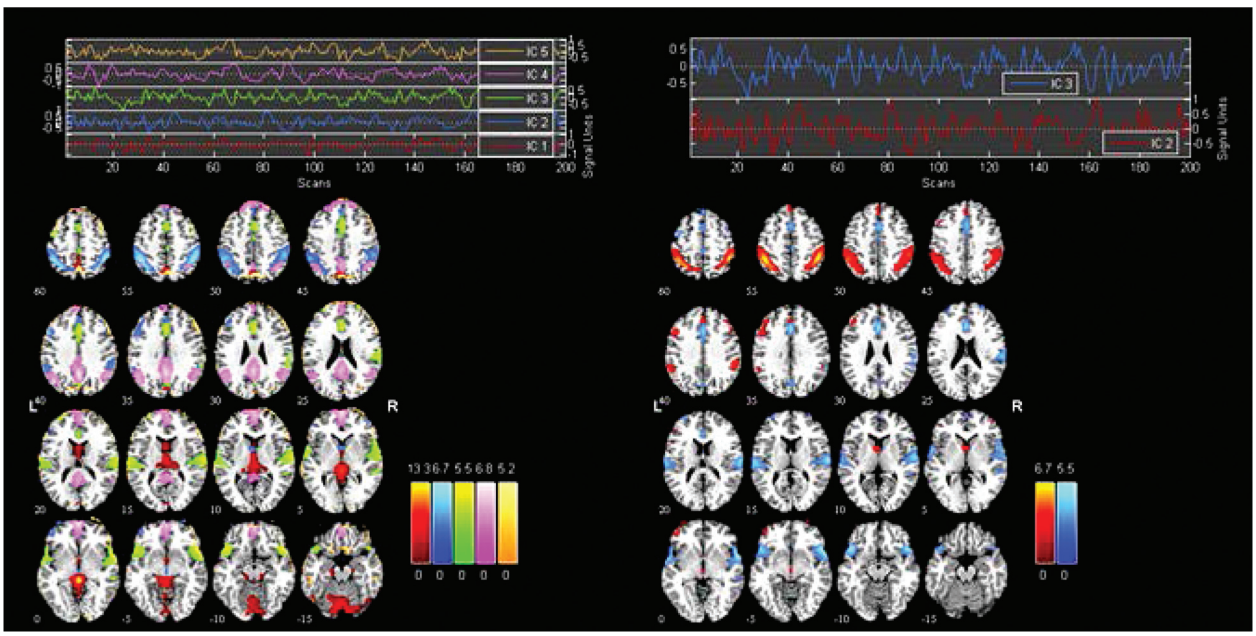
Figure 5 shows the results of model comparisons obtained from BMS for left (top) and right (bottom) hemisphere models. Model 1 = linear, Model 2 = bilinear, Model 3 and 4 = non-linear. BMS has chosen bilinear model (Figure 2(b)) as the winning model among the four models for both the left and right hemispheres. The highest value of log evidence (relative) and model posterior probability clearly indicate bilinear model as the most probable model that would best represent the effective connectivity between IPL and ITG during resting state, as far as the present model comparisons is concerned. This is supported by the minimum value of the free energy for the winning model. Table 3 summarized the BMS results for model comparisons.

The effective connectivity values for left and right hemisphere bilinear model are shown in Figure 6 together with the most probable input and modulation that have been determined. All values are in Hz (Friston et al. 2003; Kahan & Foltynie 2013) and the values in brackets are the respective probability (Friston et al. 2003) of obtaining the effective connectivity. In Bayesian framework, a value is considered to be significant if the probability (P) is larger than 0.9 (Penny et al. 2004). All probability values shown in Figure 6 are larger than 0.9 indicating significant effective connectivity, endogenous input and modulatory input values for both the right and left hemispheres. It can be seen from Figure 6 that the effective connectivity from IPL to IPG and the modulatory input that influenced the connectivity is larger than the other way around for both hemispheres.

The effective connectivity model shown in Figure 6 for left and right hemispheres indicate that the effective connection between IPL and ITG is bidirectional and bilinear in nature with the endogenous LFF influencing both the IPL and ITG and modulating the effective connectivity between them. Similar model has been chosen by BMS for both hemispheres. The endogenous input is relatively small due to the nature of LFF but is significant. Interestingly, while modulation is positive, the effective connectivity between the two regions and the endogenous input to ITG is negative for both hemispheres.

DISCUSSION

Significant activation exhibited by IPL and ITG when the brain is at rest is evident from the present fMRI findings as indicated by SPM and GIFT analyses. Parietal and temporal gyrus in which IPL and ITG are located, are two main regions that are very much involved in interpreting senses as well as in the execution of higher cognitive function and perception (Yusoff 2013; Yusoff et al. 2016). IPL and ITG activation



(a) (b)

FIGURE 4. Five independent components (IC) with their temporal response differentiated by colors as obtained from GIFT (a). IPL (red) and ITG (blue) are the two of the ICs (b)

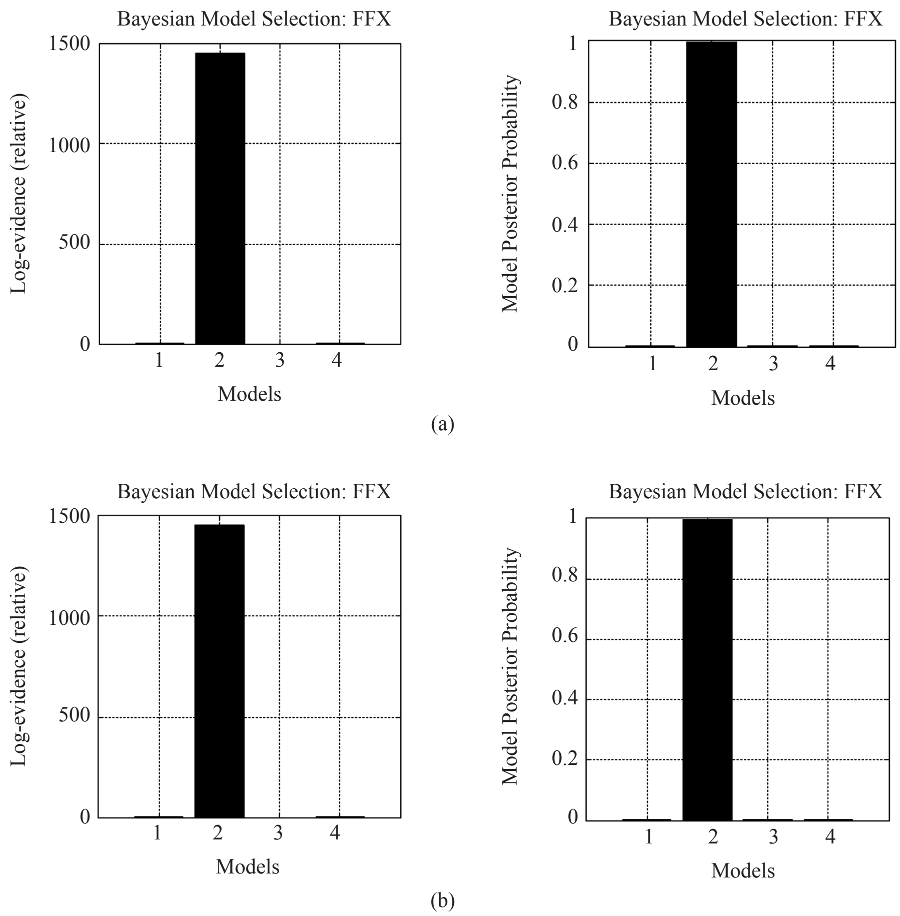


FIGURE 5. Model comparisons results using BMS; (a) left hemisphere and (b) right hemisphere

TABLE 3. Summary of BMS model comparisons results

Model	1	2	3	4
		Left hemisphere		
Log -evidence (relative)	0.0849	1100	0	0.02590
Model posterior probability	1.2664 $\times 10^{-14}$	1	1.2664 $\times 10^{-14}$	1.2664 $\times 10^{-14}$
Free energy (F) $\times 10^4$	-4.5197	-4.4097	-4.5197	-4.5197
		Right hemisphere		
Log -evidence (relative)	0.0765	1460	0	0.0207
Model posterior probability	1.2664 $\times 10^{-14}$	1	1.2664 $\times 10^{-14}$	1.2664 $\times 10^{-14}$
Free energy (F) $\times 10^4$	-4.2380	-4.0924	-4.2380	-4.2380

in resting brain reflects their additional function i.e. their roles are as important as they are in working brain, from which any injury that causes damage to these two regions may cause cognitive impairment and loss of perception, sensory and cognitive functions. Due to these vital roles of IPL and ITG (in sensory and cognitive functions), it is very important to know about how they are connected to each other and how would their connectivity be modified either in the presence of external perturbation or when the brain is at rest.

Parietal lobe is divided into three main regions which are superior parietal lobule (SPL), inferior parietal lobe (IPL) and post central gyrus (post CG). This rsfMRI study focusses on IPL because it has been found to be one of the nodes in DMN (Davey et al. 2016; Di & Biswal 2014). In a previous task-based fMRI study, the IPL, which can be divided into supra marginal gyrus and angular gyrus, has been found to play important roles in the perception of emotion in facial stimuli and interpretation of sensory information (Radua et al. 2010). Recently, it was found to be activated even though the brain is at rest (Davey et al. 2016). The findings suggested that its involvement in DMN contributes to the sense of self during resting-state fMRI. Together with prefrontal cortex (PFC), IPL is associated with self-referential condition or self-related processes

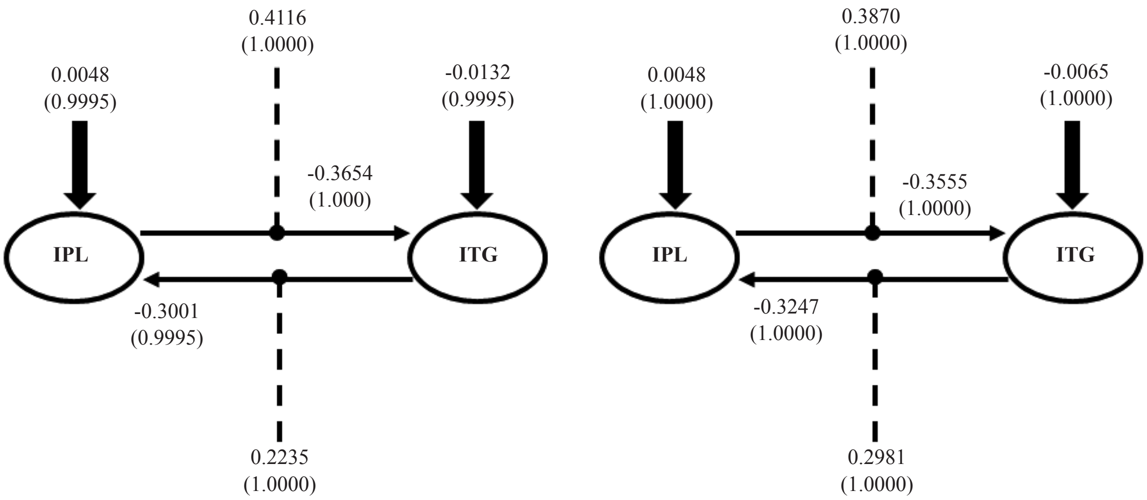


FIGURE 6. DCM for right (left) and left (right) hemisphere effective connectivity between IPL and ITG

and its activation is relatively higher for task-demanding external attention (Davey et al. 2016). In a different study, IPL is associated with memory retrieval and successful recollection (Piccoli et al. 2015), which is in line with dorsolateral prefrontal cortex (DLPFC) that has been a critical neuroanatomical region in cognitive tasks requiring attention, manipulation and response selection (Heinonen et al. 2016).

Temporal gyrus has three main regions which are superior temporal gyrus (STG), middle temporal gyrus (MTG) and inferior temporal gyrus (ITG). ITG processes visual stimuli of objects in the visual field and is involved with memory and memory recall to identify that object. ITG is also involved with the perception created by visual stimuli. Thus, it is suggested that ITG, which is synonymous with Brodmann Area 37, may be part of multiple neural networks (Fridriksson et al. 2012). Along with MTG, the ITG involves in language and semantic memory processing, visual perception and multimodal sensory integration (Onitsuka et al. 2004). This region has also been implicated in perceptual processing of visual objects (Soldan et al. 2010). In association with resting brain state, ITG was also suggested to be involved in sensory information processing while the participants are focused onto the visual fixation. Other than that, it is thought to be active due to some forms of mental imagery, which could possibly contributed by involuntary wandering of the participants' mind during the course of resting-state brain scan.

In constructing the dynamic causal models (DCMs), the definition of model space (Stephan et al. 2010) was considered which are as follows; 1) inference is made on model parameters of the optimal model, 2) optimum model structure is assumed to be identical across participants and 3) FFX analysis of parameter estimates will be used in model comparison. The constructed models appeared as the generative model of measured brain data which means the constructed models are forward models i.e. the models that would be able to explain how the observed data are caused.

The connectivity between IPL and ITG is similar in both the left and right hemispheres, from which bilinear model is the model of choice. It is evident (Figure 5 - left) that BMS was not in favor of the other competing models namely linear and non-linear models with model posterior probability equals 1 for bilinear model and almost 0 for the other models. The information exchange between IPL and ITG is bidirectional. This could be due to coupling function between self-referential and sensory information processing executed by both regions respectively (Davey et al. 2016). The effective connectivity values between the two regions are in hertz (Hz) which indicate the rate of change of the activity in each respective region with respect to time. This implies changes from one time point to the next. This change that takes place as time progresses explains how brain regions impact on each other's neural activity (Kahan & Foltynie 2013). The negative effective connectivity between ITG and IPL (Figure 6) implies that an increase of activity in one particular region causes a decrease of activity in another region. In another words, IPL and ITG mutually inhibited each other. At the neurophysiological level, this may be seen as a competition between self-referential (IPL) and sensory information processing (ITG). This behavior is similar to the effective connectivity between fusiform face area (FFA) and right parahippocampal place area (PPA) in which FFA and PPA exert a mutual negative influence on each other when the system is not perturbed by inputs, a process known as baseline reciprocal inhibition (Stephan et al. 2008). In a technical note introducing DCM for resting state fMRI (Friston et al. 2014), all the negative or inhibitory effective connection from prefrontal cortex (PFC) to frontal eye fields (FEF), from FEF to posterior parietal cortex (PPC) and from lateral occipital cortex (LOC) to motion sensitive area (V5) were found to be backward connections. In this study, the competitive interaction between IPL and ITG is linearly modulated by the endogenous fluctuation of the LFF. The evidence of this modulatory influence on the connections is very high (> 99%) for both connections. A higher effective connectivity (or also known as transfer of information) comes with a higher influence (modulation) on the connection. In Figure 6 it can be seen that IPL exert a greater influence on ITG judging from the larger effective connectivity from IPL to ITG and a larger modulatory values influencing the connection as compared to in the opposite direction. This is an evident of top-down process (higher order to a lower order) that occurs in the brain even in a resting brain state.

The involvement of IPL in the default mode network (DMN) comes in when participants are focusing on the internal representation of information and suppressing any external or internal distraction. Thus, the negative bidirectional effective connectivity between IPL and ITG is based on the justification that the suppressing of internal cognitive processing was possibly involved during the resting condition, in conjunction with the sensory information processing of the visual fixation.

There are a number of limitations in this study that may jeopardize the interpretation of results. They are as follows; 1) the number of participant was only 7. With reference to previous rsfMRI studies, number of participants varies between 12 (Abbott et al. 2013), 64 (Di & Biswal 2014) and 91 (Beaty et al. 2014). A sufficiently large number of participants in a study would allow for statistical inference to be made over a population. However, in this study, statistical inference was not made over a population but was made about the data obtained from the 7 participants. This was done by concatenating all the 1400 functional scans from all participants. Inference over a population of participants should be possible when more participants are added; 2) Only a few numbers of models were constructed and compared due to the main objective of this study which was to determine the types of model that would be able to explain the effective connectivity between IPL and ITG. More specific models can be constructed based on more DMN nodes (as indicated by Figure 4) and compared so that a better understanding about the effective connectivity among DMN nodes can be obtained; 3) This study used the Fourier basis set ($N_s = 4$) to model the LFF in the range of 0.01 Hz to 0.08 Hz that occurs in the brain during resting state. A wider frequency range should be possible to ensure a complete coverage of LFF. Other basis functions would also be possible to be implemented such as gamma function and finite impulse response function; 4) The estimation scheme used in this study which is stochastic (stochastic DCM) can be replaced by a recently developed scheme which is deterministic (spectral DCM) to overcome two major problems with the present estimating scheme; unconstrained inversion problem and potential differences in neuronal activity (Friston et al. 2014); 5) and finally more regions should be included in the DCM for a wider understanding of the network that exists when the brain is at rest.

CONCLUSION

This work has found that the signal from the LFF in the range of 0.01 Hz to 0.08 Hz that occurs in the brain when it is at rest has been able to be modelled and studied. It leads to activation in the DMN regions relatively highly and significantly. The brain activation results obtained by using SPM (based on mass univariate analysis) to determine the DMN are in accordance with that of GIFT (based on independent component analysis). Among the activated DMN regions obtained from GIFT are IPL and ITG. These two brain regions, which have important roles in sensory and cognitive functions as well as in perception, have been found to be bi-directionally connected with the influence that IPL has on ITG is comparatively larger than the influence of ITG on IPL indicating a larger magnitude of information transfer from IPL to ITG. The effective connectivity between the two is negative indicating mutual inhibitory process that occurs during the information transfer between IPL and ITG. The connections are however positively modulated by the LFF which also acts as an endogenous input into the system. Bilinear causal model with an internal modulatory input to the regions and connections has been found to be the optimal model among the four competing models. The evidence of the presence of this modulatory input is very high (> 90%) for both connections. In another words, this model has the best balance between accuracy (fit) and difficulty, at least in the context of the present study.

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